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目　录

《Science》2011.2.4 第 331 卷 6017 期

内容精选

延伸阅读

《Science》2011.2.11 第 331 卷 6018 期

内容精选

延伸阅读

《Science》2011.2.18 第 331 卷 6019 期

内容精选

延伸阅读

《Science》2011.2.25 第 331 卷 6020 期

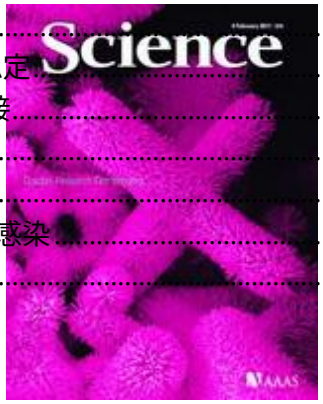
内容精选

延伸阅读

2011 年 4 月 10 日

《Science》2011.2.4 第 331 卷 6017 期

内容精选



延伸阅读

内容精选

1. 水蚤基因组测序完成

标题：The Ecoresponsive Genome of Daphnia pulex

作者：Colbourne,John K.; et al.

来源出版物：Science 卷：331 期：6017 页：555-561 时间：4 February 2011

摘要：We describe the draft genome of the microcrustacean Daphnia pulex, which is only 200 megabases and contains at least 30,907 genes. The high gene count is a consequence of an elevated rate of gene duplication resulting in tandem gene clusters. More than a third of Daphnia's genes have no detectable homologs in any other available proteome, and the most amplified gene families are specific to the Daphnia lineage. The coexpansion of gene families interacting within metabolic pathways suggests that the maintenance of duplicated genes is not random, and the analysis of gene expression under different environmental conditions reveals that numerous paralogs acquire divergent expression patterns soon after duplication. Daphnia-specific genes, including many additional loci within sequenced regions that are otherwise devoid of annotations, are the most responsive genes to ecological challenges.

（水蚤成为第一种基因组被测序的甲壳类动物）科学家们已经对蚤状蚤水蚤的基因组完成了测序。蚤状蚤是环境科学和其他生物学领域的一种重要的模式生物。这也是基因组第一个被测序的甲壳类动物。John Colbourne 及其一个国际性的研究团队报告说，这种极其细小的淡水虾的亲缘生物的基因组中充满了各种基因。它有着比其他已知基因序列要更多的基因，而且它有着相对较少的非编码 DNA。其许多基因是重复的，有超过三分之一的基因看来是水蚤世系所独有的。这些新的基因中有些是有着最丰富拷贝的基因。水蚤是淡水食物链中的基石物种，而它们的生物学特性对科学实验非常有帮助。

水蚤通体透明，其生命周期短暂，而且很容易被克隆。它们还非常容易地对它们的环境变化作出反应。例如，在对掠食者释放的化学物质作出反应时，它们会长出诸如保护性的尾刺、盔甲和颈齿等。它们还可适应范围很广的酸度、毒素、氧气浓度、食物质量和温度。

2. 通过将芳香侧链置于 N-糖基化反转中使蛋白质天然态稳定

标题：Protein Native-State Stabilization by Placing Aromatic Side Chains in N-Glycosylated Reverse Turns

作者：Culyba,Elizabeth K.; et al.

来源出版物：Science 卷：331 期：6017 页：571-575 时间：4 February 2011

摘要：If they could be easily exfoliated, layered materials would become a diverse source of two-dimensional crystals whose properties would be useful in applications ranging from electronics to energy storage. We show that layered compounds such as MoS2, WS2, MoSe2, MoTe2, TaSe2, NbSe2, NiTe2, BN, and Bi2Te3 can be efficiently dispersed in common solvents and can be deposited as individual flakes or formed into films. Electron microscopy strongly suggests that the material is exfoliated into individual layers. By blending this material with suspensions of other nanomaterials or polymer solutions, we can prepare hybrid dispersions or composites, which can be cast into films. We show that WS2 and MoS2 effectively reinforce polymers, whereas WS2/carbon nanotube hybrid films have high conductivity, leading to promising thermoelectric properties.

3. 平移式暂停确保 XBP1u mRNA 的膜定位和细胞质的剪接

标题：Translational Pausing Ensures Membrane Targeting and Cytoplasmic Splicing of XBP1u mRNA

作者：Yanagitani,Kota; et al.

来源出版物：Science 卷：331 期：6017 页：586-589 时间：4 February 2011

摘要：Upon endoplasmic reticulum (ER) stress, an endoribonuclease, inositol-requiring enzyme-1¦Á splices the precursor unspliced form of X-box–binding protein 1 messenger RNA (XBP1u mRNA) on the ER membrane to yield an active transcription factor (XBP1s), leading to the alleviation of the stress. The nascent peptide encoded by XBP1u mRNA drags the mRNA–ribosome–nascent chain (R-RNC) complex to the membrane for efficient cytoplasmic splicing. We found that translation of the XBP1u mRNA was briefly paused to stabilize the R-RNC complex. Mutational analysis of XBP1u revealed an evolutionarily conserved peptide module at the carboxyl terminus that was responsible for the translational pausing and was required for the efficient targeting and splicing of the XBP1u mRNA. Thus, translational pausing may be used for unexpectedly diverse cellular processes in mammalian cells.

4. 蛋白质壳的定向演变

标题：Directed Evolution of a Protein Container

作者：Wörsdörfer,Bigna; et al.

来源出版物：Science 卷：331 期：6017 页：589-592 时间：4 February 2011

摘要：Confinement of enzymes in protein nanocompartments represents a potentially powerful strategy for controlling catalytic activity in cells. By using a simple electrostatically based tagging system for protein encapsulation, we successfully sequestered HIV protease, a toxic enzyme when produced cytoplasmically, within an engineered lumazine synthase capsid. The growth advantage resulting from protecting the Escherichia coli host from the protease enabled directed evolution of improved capsids. After four rounds of mutagenesis and selection, we obtained a variant with a 5- to 10-fold higher loading capacity than the starting capsid, which permitted efficient growth even at high intracellular concentrations of HIV protease. The superior properties of the evolved capsid can be ascribed to multiple mutations that increase the net negative charge on its luminal surface and thereby enhance engineered Coulombic interactions between host and guest. Such structures could be used for diverse biotechnological applications in living cells.

5. 胰腺癌和其他上皮癌附属重复序列的异常表达

标题：Aberrant Overexpression of Satellite Repeats in Pancreatic and Other Epithelial Cancers

作者：Ting,David T.; et al.

来源出版物：Science 卷：331 期：6017 页：593-596 时间：4 February 2011

摘要：Satellite repeats in heterochromatin are transcribed into noncoding RNAs that have been linked to gene silencing and maintenance of chromosomal integrity. Using digital gene expression analysis, we showed that these transcripts are greatly overexpressed in mouse and human epithelial cancers. In 8 of 10 mouse pancreatic ductal adenocarcinomas (PDACs), pericentromeric satellites accounted for a mean 12% (range 1 to 50%) of all cellular transcripts, a mean 40-fold increase over that in normal tissue. In 15 of 15 human PDACs, alpha satellite transcripts were most abundant and HSATII transcripts were highly specific for cancer. Similar patterns were observed in cancers of the lung, kidney, ovary, colon, and prostate. Derepression of satellite transcripts correlated with overexpression of the long interspersed nuclear element 1 (LINE-1) retrotransposon and with aberrant expression of neuroendocrine-associated genes proximal to LINE-1 insertions. The overexpression of satellite transcripts in cancer may reflect global alterations in heterochromatin silencing and could potentially be useful as a biomarker for cancer detection.

6. 冈比亚按蚊的一种隐秘亚群极易受到人类疟疾寄生虫的感染

标题：A Cryptic Subgroup of Anopheles gambiae Is Highly Susceptible to Human

Malaria Parasites

作者：Riehle,Michelle M.; et al.

来源出版物：Science 卷：331 期：6017 页：596-598 时间：4 February 2011

摘要：Population subgroups of the African malaria vector Anopheles gambiae have not been comprehensively characterized owing to the lack of unbiased sampling methods. In the arid savanna zone of West Africa, where potential oviposition sites are scarce, widespread collection from larval pools in the peridomestic human habitat yielded a comprehensive genetic survey of local A. gambiae population subgroups, independent of adult resting behavior and ecological preference. A previously unknown subgroup of exophilic A. gambiae is sympatric with the known endophilic A. gambiae in this region. The exophilic subgroup is abundant, lacks differentiation into M and S molecular forms, and is highly susceptible to infection with wild Plasmodium falciparum. These findings might have implications for the epidemiology of malaria transmission and control.

（蚊子新种引发人们对疟疾的担心）研究人员说，人们发现了一个从前未被分类的蚊子，其基因与已知的蚊虫亚群截然不同，而且它们对疟原虫高度易感。这些可能都与疟疾的传播和控制有关系。Michelle Riehle 及其同事在 4 年中从布基纳法索的靠近村庄的池塘中收集了蚊子的标本，并发现了冈比亚按蚊的一个亚群。该亚群与从前所收集发现的任何蚊子都不同。研究人员提示，这是因为在过去所收集到的用于研究的蚊子几乎全部都是从人的居所内捕捉到的，因为居所内的蚊子容易被抓到。这些居住在户内的蚊子会展现某些行为以及对疟原虫的易感性，这使得它们得以与户外的蚊子区分开来，而研究人员认为，绝大多数的疟疾是通过室内种类的蚊子传播的。然而，从前的像在 20 世纪 70 年代在尼日利亚实施的 Garki 计划这样的控制疟疾的措施失败了，因为与户内蚊子在基因上迥异的户外蚊子使得疟疾的传播得以持续，尽管户内杀虫剂已经得到了广泛的使用。Riehle 及其同事在实验室中培育了多代的独特的冈比亚按蚊亚群，并发现它比记录在案的居住在户内种类的蚊子更容易感染恶性疟原虫。根据这些发现，研究人员提示，这一新的蚊子亚群可能在进化上是相当年轻的。

7. 轴突传导期间动作电位的调制

标题：Action-Potential Modulation During Axonal Conduction

作者：Sasaki,Takuya; et al.

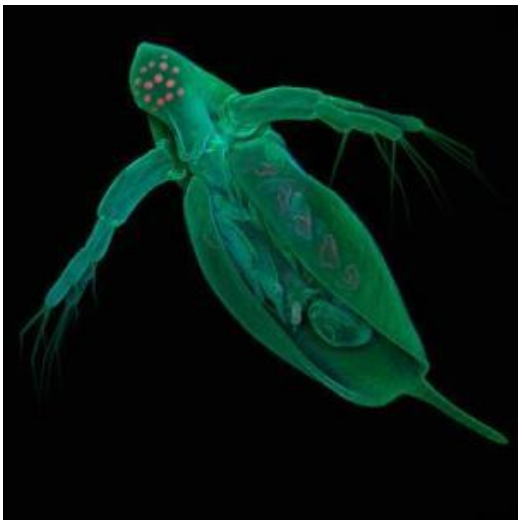
来源出版物：Science 卷：331 期：6017 页：599-601 时间：4 February 2011

摘要：Once initiated near the soma, an action potential (AP) is thought to propagate autoregeneratively and distribute uniformly over axonal arbors. We challenge this classic view by showing that APs are subject to waveform modulation while they travel down axons. Using fluorescent patch-clamp pipettes, we recorded APs from axon branches of hippocampal CA3 pyramidal neurons ex vivo. The waveforms of axonal APs increased in width in response to the local application of glutamate and an adenosine A1 receptor antagonist to the axon shafts, but not to other unrelated axon branches. Uncaging of calcium in periaxonal astrocytes caused AP broadening through ionotropic glutamate receptor activation. The

broadened APs triggered larger calcium elevations in presynaptic boutons and facilitated synaptic transmission to postsynaptic neurons. This local AP modification may enable axonal computation through the geometry of axon wiring.

延伸阅读

科学家完成水蚤基因组测序



水蚤（图片来源：Jan Michels, Christian-Albrechts-Universitaet zu Kiel）

近日由美国印第安纳州大学科学家领导的一个由多家研究机构科研人员组成的国际研究小组完成了对水蚤的基因组测序，相关研究论文在线发表在 2011 年 2 月 4 日的《科学》（*Science*）杂志上。这是科学家们第一次对甲壳类动物进行基因组测序。

水蚤俗称水跳蚤，是淡水食物链中的基石物种。由于其具有的独特生物学特性，使其成为了目前获得美国国立卫生研究院批准用于环境科学和其他生物学领域研究的一种重要的模式生物。水蚤通体透明，其生命周期短暂，并且很容易被克隆。它们还非常容易地对它们的环境变化作出反应。例如，在对掠食者释放的化学物质做出反应时，它们会长出诸如保护性的尾刺、盔甲和颈齿等。它们还可适应范围很广的酸度、毒素、氧气浓度、食物质量和温度。这些生物学特性对于科学实验非常有帮助。

这一国际性研究团队的负责人是来自美国印第安纳大学基因组学和生物信息学中心的基因组学主管 John Colbourne。John Colbourne 等在新研究中发现，这种极其细小的淡水虾的亲缘生物的基因组中充满了各种基因。它有着比其他已知的所有动物的基因序列还要多的基因。研究人员证实，相比人类包含 23000 个左右的基因，在水蚤的 DNA 中包含了大约 31000 个基因；而且它只有相对较少的非编码 DNA。研究人员发现水蚤能拥有如此多的基因数量主要是因为水蚤具有很高的基因重复率。其基因重复率大概是其他无脊椎动物的三倍，比人类多出 30%。并且其中超过三分之一的基因为水蚤世系所独有，这对科学界而言无疑意味着全新的科学领域。

进而科学家们对水蚤基因家族共表达在代谢信号途径中的相互作用开展进一步研究证实这些重复基因并非随机存在。不同环境条件下的基因表达分析结果表明，大量的

旁系同源基因在发生基因重复后获得了不同的表达模式。那些水蚤特异性基因均对生态环境的改变极度敏感。

这一研究标志着科学家们第一次获得了甲壳动物的完整基因组序列。研究结果表明，这个看似简单，有着透明身体、关节和四肢、复眼结构以及简单神经和循环系统的小生物不仅拥有非常庞大的基因组，并且具有很多神奇之处。

文章的作者表示他们希望对水蚤基因组的测序能使人们更好地理解生物，特别是生活在淡水中的那些生物，是如何对环境变化作出反应的。

作者：John K. Colbourne 来源：《科学》

http://paper.sciencenet.cn/htmlpaper/20112141014169514977.shtm

《Science》2011.2.11 第 331 卷 6018 期

内容精选

延伸阅读

内容精选

1. 真核细胞 40S 核糖体亚基与起始因子 1 化合物的晶体结构

标题：Crystal Structure of the Eukaryotic 40S Ribosomal Subunit in Complex with Initiation Factor 1

作者：Rabl,Julius; et al.

来源出版物：Science 卷：331 期：6018 页：730-736 时间：11 February 2011

摘要：Eukaryotic ribosomes are substantially larger and more complex than their bacterial counterparts. Although their core function is conserved, bacterial and eukaryotic protein synthesis differ considerably at the level of initiation. The eukaryotic small ribosomal subunit (40S) plays a central role in this process; it binds initiation factors that facilitate scanning of messenger RNAs and initiation of protein synthesis. We have determined the crystal structure of the Tetrahymena thermophila 40S ribosomal subunit in complex with eukaryotic initiation factor 1 (eIF1) at a resolution of 3.9 angstroms. The structure reveals the fold of the entire 18S ribosomal RNA and of all ribosomal proteins of the 40S subunit, and defines the interactions with eIF1. It provides insights into the eukaryotic-specific aspects of protein synthesis, including the function of eIF1 as well as signaling and regulation mediated by the ribosomal proteins RACK1 and rpS6e.

2. 南方古猿阿法种脚部完整的第四跖骨和弓形足

标题：Complete Fourth Metatarsal and Arches in the Foot of Australopithecus afarensis

作者：Ward,Carol V.; et al.

来源出版物：Science 卷：331 期：6018 页：750-753 时间：11 February 2011

摘要：The transition to full-time terrestrial bipedality is a hallmark of human evolution. A key correlate of human bipedalism is the development of longitudinal and transverse arches of the foot that provide a rigid propulsive lever and critical shock absorption during striding bipedal gait. Evidence for arches in the earliest well-known Australopithecus species, A. afarensis, has long been debated. A complete fourth metatarsal of A. afarensis was recently discovered at Hadar, Ethiopia. It exhibits torsion of the head relative to the base, a direct correlate of a transverse arch in humans. The orientation of the proximal and distal ends of the bone reflects a longitudinal arch. Further, the deep, flat base and tarsal facets imply that its midfoot had no ape-like midtarsal break. These features show that the A. afarensis foot was functionally like that of modern humans and support the hypothesis that this species was a committed terrestrial biped.

（足骨提示 Lucy 的亲族具有行走的弓形足）一个人类早期亲族南方古猿阿法种的足骨提示，这些原始人具有像我们这样的强直的弓形足。这些发现支持这样的假说，即南方古猿阿法种主要是一种直立的行走动物，而不是一个更为灵动的还可在树丛中通行的动物。南方古猿阿法种生活在距今 370 万年至 290 万年前，而其最著名的代表就是 Lucy，其部分的骨骼显示，她可直立行走。研究人员长期以来一直在辩论南方古猿阿法种究竟在什么程度上属于双足动物，然而，他们对这一问题的了解因为南方古猿阿法种的足部中段的关键骨的化石记录稀少而受到妨碍。Carol Ward 及其同事如今描述了一个来自埃塞俄比亚 Hadar 的一个新发现的足骨。他们称该足骨的保存近乎完美。该骨头是一个完整的第四跖骨（即连接脚趾与足底的长骨之一）。该骨头与猿的骨头相比有数个与现代人的脚类似的特征。例如，其两端是相互扭曲的，而且其足底与脚趾是以一个相对较锐的角度倾斜的。这只脚以其形成良好的足弓应该有着足够的强硬度以蹬离地面，且其也有足够的弹性来吸收冲击。文章的作者说，该化石因而提示，南方古猿阿法种的脚已经从握抓结构而完全转化成为那种像人这样便于行走和奔跑的两脚。

3. 鸟类胚胎的实例鉴定出其翅膀的指骨包括了 D1、D2 和 D3 指

标题：Embryological Evidence Identifies Wing Digits in Birds as Digits 1, 2, and 3

作者：Tamura,Koji; et al.

来源出版物：Science 卷：331 期：6018 页：753-757 时间：11 February 2011

摘要：Splicing of mammalian precursor transfer RNA (tRNA) molecules involves two enzymatic steps. First, intron removal by the tRNA splicing endonuclease generates separate 5¡äand 3¡äexons. In animals, the second step predominantly entails direct exon ligation by an elusive RNA ligase. Using activity-guided purification of tRNA ligase from HeLa cell extracts, we identified HSPC117, a member of the UPF0027 (RtcB) family, as the essential

subunit of a tRNA ligase complex. RNA interference–mediated depletion of HSPC117 inhibited maturation of intron-containing pre-tRNA both in vitro and in living cells. The high sequence conservation of HSPC117/RtcB proteins is suggestive of RNA ligase roles of this protein family in various organisms.

（小鸡“指”之谜结案）四个肢体的动物，从鸟类到人类，在其发育时都服从于 5 个指趾的构造（例如 5 个手指），尽管有某些物种会在其进化中，个别的指趾会丧失或迁移。现在，研究人员已经解开了长期存在的鸟类翼指的谜团。该谜团令古生物学家和胚胎学家的观点长期分裂，前者声称鸟的翅膀中包括了 D1、D2 和 D3 指，而后者说，鸟类的指包括了 D2、D3 和 D4。作为参考，D1 指相当于人类的拇指、D2 指表示食指，等等。据 Koji Tamura 披露，鸟类翅膀的指骨确实是 D1、D2 和 D3，但它们是在 D2、D3 和 D4 的位置上发育起来的。这一发现披露了鸟类指骨分类中的一个独特的发育机制，而这一机制不符合标准的 5 指构造。通过研究小鸡胚胎的翼指的发育，并将其与小鼠模型进行比较，这些研究人员可以最后确定小鸡前肢的最后指为 D3。然而，在小鸡的指骨发生专门化之前，Tamura 及其同事注意到，D3 指骨开始在 D4 的位置发育。他们说，这一发育期间的位置上的变化反映了某些像鸟样的恐龙在数百万年前所经历的前肢形态学的缓慢进化。因此，根据研究人员的说法，对现代翼指的进化上的描述可以在小鸡的胚胎发育中得到见证。

4. 肌球蛋白 VIIa 尾部 MyTH4-FERM 域的结构和人类失聪相关

标题：Structure of MyTH4-FERM Domains in Myosin VIIa Tail Bound to Cargo

作者：Wu,Lin; et al.　P. 757-760

来源出版物：Science　卷：331　期：6018　页：757-760　时间：11 February 2011

摘要：The unconventional myosin VIIa (MYO7A) is one of the five proteins that form a network of complexes involved in formation of stereocilia. Defects in these proteins cause syndromic deaf-blindness in humans [Usher syndrome I (USH1)]. Many disease-causing mutations occur in myosin tail homology 4–protein 4.1, ezrin, radixin, moesin (MyTH4-FERM) domains in the myosin tail that binds to another USH1 protein, Sans. We report the crystal structure of MYO7A MyTH4-FERM domains in complex with the central domain (CEN) of Sans at 2.8 angstrom resolution. The MyTH4 and FERM domains form an integral structural and functional supramodule binding to two highly conserved segments (CEN1 and 2) of Sans. The MyTH4-FERM/CEN complex structure provides mechanistic explanations for known deafness-causing mutations in MYO7A MyTH4-FERM. The structure will also facilitate mechanistic and functional studies of MyTH4-FERM domains in other myosins.

（蛋白复合物含有人类失聪的秘密）研究人员捕捉到了一个众所周知的蛋白化合物的画面，当该化合物发生突变时，常常会导致人类的失聪。他们说，这一分辨率为 2.8 埃的晶体结构为许多致病性突变提供了一个基础机制。Lin Wu 及其一个来自香港的研究团队捕捉到了该画面，它显示了在肌球蛋白 VIIa 的尾部的与另外一个叫做 Sans 的蛋白相附着的某组特别的氨基酸。他们说，肌球蛋白 VIIa 和 Sans 是 5 个蛋白中的两个，

这些蛋白会形成一个对内耳细胞的完整性来说至关重要的复合物，而肌球蛋白 VIIa 的突变可以解释高达一半的所有的尤塞氏综合征-I 的病例，这是一种引起耳聋的遗传性疾病。很明显，两个不同的氨基酸组（MyTH4 域和 FERM 域）会在肌球蛋白 VIIa 的尾部形成一个“超级模块”，它接着会与 Sans 蛋白的高度保守的区域结合。

5. HSPC117 是人类 tRNA 拼接连接酶化合物的一个基本亚基

标题：HSPC117 Is the Essential Subunit of a Human tRNA Splicing Ligase Complex

作者：Popow,Johannes; et al. P. 760-764

来源出版物：Science 卷：331 期：6018 页：760-764 时间：11 February 2011

摘要：Splicing of mammalian precursor transfer RNA (tRNA) molecules involves two enzymatic steps. First, intron removal by the tRNA splicing endonuclease generates separate 5¡ä and 3¡äexons. In animals, the second step predominantly entails direct exon ligation by an elusive RNA ligase. Using activity-guided purification of tRNA ligase from HeLa cell extracts, we identified HSPC117, a member of the UPF0027 (RtcB) family, as the essential subunit of a tRNA ligase complex. RNA interference–mediated depletion of HSPC117 inhibited maturation of intron-containing pre-tRNA both in vitro and in living cells. The high sequence conservation of HSPC117/RtcB proteins is suggestive of RNA ligase roles of this protein family in various organisms.

6. 人类细胞中的蛋白质组半衰期动力学

标题：Proteome Half-Life Dynamics in Living Human Cells

作者：Eden, Eran; et al.

来源出版物：Science 卷：331 期：6018 页：764-768 时间：11 February 2011

摘要：Cells remove proteins by two processes: degradation and dilution due to cell growth. The balance between these basic processes is poorly understood. We addressed this by developing an accurate and noninvasive method for measuring protein half-lives, called “bleach-chase,” that is applicable to fluorescently tagged proteins. Assaying 100 proteins in living human cancer cells showed half-lives that ranged between 45 minutes and 22.5 hours. A variety of stresses that stop cell division showed the same general effect: Long-lived proteins became longer-lived, whereas short-lived proteins remained largely unaffected. This effect is due to the relative strengths of degradation and dilution and suggests a mechanism for differential killing of rapidly growing cells by growth-arresting drugs. This approach opens a way to understand proteome half-life dynamics in living cells.

7. 肾上腺醛固酮腺瘤和遗传性高血压的钾离子通道基因突变

标题：K+ Channel Mutations in Adrenal Aldosterone-Producing Adenomas and Hereditary Hypertension

作者：Choi,Murim; et al.

来源出版物：Science 卷：331 期：6018 页：768-772 时间：11 February 2011

摘要：Endocrine tumors such as aldosterone-producing adrenal adenomas (APAs), a cause of severe hypertension, feature constitutive hormone production and unrestrained cell proliferation; the mechanisms linking these events are unknown. We identify two recurrent somatic mutations in and near the selectivity filter of the potassium (K+) channel KCNJ5 that are present in 8 of 22 human APAs studied. Both produce increased sodium (Na+) conductance and cell depolarization, which in adrenal glomerulosa cells produces calcium (Ca2+) entry, the signal for aldosterone production and cell proliferation. Similarly, we identify an inherited KCNJ5 mutation that produces increased Na+ conductance in a Mendelian form of severe aldosteronism and massive bilateral adrenal hyperplasia. These findings explain pathogenesis in a subset of patients with severe hypertension and implicate loss of K+ channel selectivity in constitutive cell proliferation and hormone production.

8. 利什曼原虫 RNA 病毒控制着粘膜皮肤利什曼病的严重程度

标题：Leishmania RNA Virus Controls the Severity of Mucocutaneous Leishmaniasis

作者： Ives,Annette; et al.

来源出版物：Science 卷：331 期：6018 页：775-778 时间：11 February 2011

摘要：Mucocutaneous leishmaniasis is caused by infections with intracellular parasites of the Leishmania Viannia subgenus, including Leishmania guyanensis. The pathology develops after parasite dissemination to nasopharyngeal tissues, where destructive metastatic lesions form with chronic inflammation. Currently, the mechanisms involved in lesion development are poorly understood. Here we show that metastasizing parasites have a high Leishmania RNA virus–1 (LRV1) burden that is recognized by the host Toll-like receptor 3 (TLR3) to induce proinflammatory cytokines and chemokines. Paradoxically, these TLR3-mediated immune responses rendered mice more susceptible to infection, and the animals developed an increased footpad swelling and parasitemia. Thus, LRV1 in the metastasizing parasites subverted the host immune response to Leishmania and promoted parasite persistence.

9. 调节过的解聚集作用允许脑膜炎奈瑟菌传播到新的宿主细胞并穿过上皮细胞迁移

标题：Posttranslational Modification of Pili upon Cell Contact Triggers N. meningitidis Dissemination

作者：Chamot-Rooke,Julia; et al.

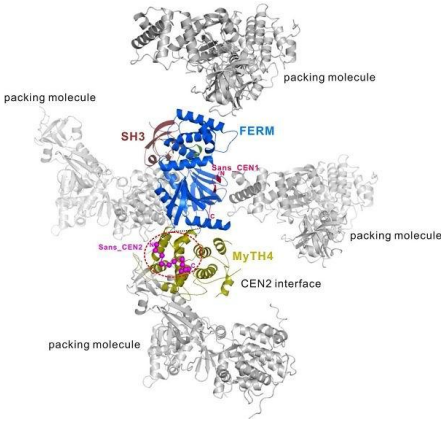
来源出版物：Science 卷：331 期：6018 页：778-782 时间：11 February 2011

摘要：The Gram-negative bacterium Neisseria meningitidis asymptomatically colonizes the throat of 10 to 30% of the human population, but throat colonization can also act as the port of entry to the blood (septicemia) and then the brain (meningitis). Colonization is mediated by filamentous organelles referred to as type IV pili, which allow the formation of

bacterial aggregates associated with host cells. We found that proliferation of N. meningitidis in contact with host cells increased the transcription of a bacterial gene encoding a transferase that adds phosphoglycerol onto type IV pili. This unusual posttranslational modification specifically released type IV pili-dependent contacts between bacteria. In turn, this regulated detachment process allowed propagation of the bacterium to new colonization sites and also migration across the epithelium, a prerequisite for dissemination and invasive disease.

延伸阅读

1.研究解析肌动蛋白 7a 晶体结构



利用上海光源生物大分子光束线站(BL17U)采集得到的数据解析的肌动蛋白 7a 与 Sans 蛋白复合物晶体结构

上海光源用户香港科技大学（科大）生命科学部讲座教授张明杰及他的研究团队在 2011 年 2 月 11 日《科学》（Science 2011, 331, 757）杂志上发表了题为“Structure of MyTH4-FERM Domains in Myosin VIIa Tail Bound to Cargo”的论文，该论文研究了肌动蛋白 7a 的突变如何导致先天性失聪失明。

根据医学统计数字，听力障碍在新生婴儿中相当普遍©©每 1,000 个新生婴儿中就有几个病例。在失聪或弱听的儿童中，有 3%至 6%是 Usher 综合症患者。Usher 综合症是一种基因失调的病症，它会导致病人在生命不同阶段蒙受不同程度的听力或视力丧失。

肌动蛋白 7a 是一类在细胞体内负责运输的分子，它的功能对于人类听力毛细胞和眼睛的发育尤为重要。肌动蛋白 7a 的基因变异可以导致严重的失聪和失明，这就是常见于新生婴儿和儿童的 Usher 综合症。在所有 Usher1 综合症患者中，约一半是由肌动蛋白 7a 变异所引起的。

经过大批量遗传学调查，已发现 160 余种肌动蛋白 7a 基因变异会导致失聪。同时，一些能够与肌动蛋白 7a 相互结合的蛋白的基因突变也会造成 Usher 综合症。尽管有了这些信息，但是肌动蛋白 7a 以及其运输物体的变异为何会造成失聪失明，至今还是一个谜团。

张明杰教授及他的研究团队，利用在上海光源生物大分子晶体学线站 BL17U 采集的晶体 X 光衍射数据，成功解析了肌动蛋白 7a 与 Sans（另外一种可导致 Usher 综合症的蛋白质，其功能主要是充当桥连蛋白，将肌动蛋白 7a 的运输物体与其链接在一起）蛋白质复合物 2.8 埃分辨晶体结构。结合核磁共振技术得到的结果，解释了肌动蛋白 7a 在不同细胞中是如何进行运输，也解释了其在内耳细胞中是如何维持耳毛细胞结构的。

非常重要的是，肌动蛋白 7a 与 Sans 的分子结构，直观清晰地解释了在肌动蛋白 7a 的“装货区域”发现的大量致病突变是如何影响到其正常的运载功能。同时，由于蛋白质结构的相似性，这项发现同样可以用于解释在肌动蛋白 15a 上发现的许多致病突变而造成非综合症型耳聋性遗传病。

作者：张明杰等 来源：《科学》

http://paper.sciencenet.cn/htmlpaper/20112171482059815058.shtm

2. 日本新研究佐证“鸟类起源于恐龙”学说

日本一项最新研究发现，鸟类翅膀内 3 根趾骨的位置相当于人类的拇指、食指和中指，与被认为是鸟类祖先的兽脚类恐龙前肢具有相同形态。这一发现为“鸟类起源于恐龙”的学说提供了决定性证据。

长期以来，对于鸟类是否起源于恐龙，古生物学家和发育生物学家持有不同看法。从古生物学角度来看，由于兽脚类恐龙前肢的趾骨与鸟类翅膀的趾骨形态相近，并且近年来接连出土具有羽毛结构的恐龙化石，这些证据使得“鸟类起源于恐龙”学说显得非常有说服力。

从发育生物学角度看，兽脚类恐龙前肢 3 根趾骨的位置相当于人类的拇指、食指和中指；而鸟类翅膀内 3 根趾骨的位置过去一直被认为相当于人类的食指、中指和无名指。兽脚类恐龙前肢和鸟类翅膀内 3 根趾骨位置的差异使得发育生物学家对鸟类起源持不同看法，有学者认为鸟类可能是由更古老的爬虫类进化而来。

日本东北大学教授田村宏治领导的研究小组在 2 月 11 日的美国《科学》杂志网络版上报告说，他们利用鸡的受精卵调查了从受精 3 天至 3 天半时间内开始的发育过程。结果发现，在发育初期，鸟类翅膀在相当于人类食指、中指和无名指的位置分别有作为趾骨原型的细胞群存在，按照原有观点，这些细胞群将发育成“食指”、“中指”和“无名指”。但研究小组发现，这些细胞群真正发育成趾骨的时候，却相继偏离最初位置，在与兽脚类恐龙的前肢 3 根趾骨相同的位置发育成了趾骨，这 3 个位置相当于人类的拇指、食指和中指。

研究小组认为，这一“偏离”现象的发现可以消除古生物学家和发育生物学家在鸟类起源问题上的不同看法，成为支持“鸟类起源于恐龙”的一个决定性证据。日本国立科学博物馆主任研究员真锅真指出：“这一发现从发育生物学角度阐明了利用化石无法弄清的进化过程，具有重要意义。”

作者：Koji Tamura 来源：《科学》

http://news.sciencenet.cn/htmlnews/2011/2/243759.shtm

《Science》2011.2.18 第 331 卷 6019 期

内容精选

延伸阅读

内容精选

1. 子宫上皮细胞中孕激素的抗增殖作用是通过 Hand2介导的

标题：The Antiproliferative Action of Progesterone in Uterine Epithelium Is Mediated by Hand2

作者：Li,Quanxi; et al.

来源出版物：Science 卷：331 期：6019 页：912-916 时间：18 February 2011

摘要：During pregnancy, progesterone inhibits the growth-promoting actions of estrogen in the uterus. However, the mechanism for this is not clear. The attenuation of estrogen-mediated proliferation of the uterine epithelium by progesterone is a prerequisite for successful implantation. Our study reveals that progesterone-induced expression of the basic helix-loop-helix transcription factor Hand2 in the uterine stroma suppresses the production of several fibroblast growth factors (FGFs) that act as paracrine mediators of mitogenic effects of estrogen on the epithelium. In mouse uteri lacking Hand2, continued induction of these FGFs in the stroma maintains epithelial proliferation and stimulates estrogen-induced pathways, resulting in impaired implantation. Thus, Hand2 is a critical regulator of the uterine stromal-epithelial communication that directs proper steroid regulation conducive for the establishment of pregnancy.

2. XY 拟常染色体区的截然不同性质是男减数分裂的关键

标题：Distinct Properties of the XY Pseudoautosomal Region Crucial for Male Meiosis

作者：Kauppi,Liisa; et al.

来源出版物：Science 卷：331 期：6019 页：916-920 时间：18 February 2011

摘要：Meiosis requires that each chromosome find its homologous partner and undergo at least one crossover. X-Y chromosome segregation hinges on efficient crossing-over in a very small region of homology, the pseudoautosomal region (PAR). We find that mouse PAR DNA occupies unusually long chromosome axes, potentially as shorter chromatin loops,

predicted to promote double-strand break (DSB) formation. Most PARs show delayed appearance of RAD51/DMC1 foci, which mark DSB ends, and all PARs undergo delayed DSB-mediated homologous pairing. Analysis of Spo11¦Âisoform–specific transgenic mice revealed that late RAD51/DMC1 foci in the PAR are genetically distinct from both early PAR foci and global foci and that late PAR foci promote efficient X-Y pairing, recombination, and male fertility. Our findings uncover specific mechanisms that surmount the unique challenges of X-Y recombination.

3. 脊髓损伤后微管稳定减少疤痕并促使轴突再生

标题：Microtubule Stabilization Reduces Scarring and Causes Axon Regeneration After Spinal Cord Injury

作者：Hellal,Farida; et al.

来源出版物：Science 卷：331 期：6019 页：928-931 时间：18 February 2011

摘要：Hypertrophic scarring and poor intrinsic axon growth capacity constitute major obstacles for spinal cord repair. These processes are tightly regulated by microtubule dynamics. Here, moderate microtubule stabilization decreased scar formation after spinal cord injury in rodents through various cellular mechanisms, including dampening of transforming growth factor–¦Âsignaling. It prevented accumulation of chondroitin sulfate proteoglycans and rendered the lesion site permissive for axon regeneration of growth-competent sensory neurons. Microtubule stabilization also promoted growth of central nervous system axons of the Raphe-spinal tract and led to functional improvement. Thus, microtubule stabilization reduces fibrotic scarring and enhances the capacity of axons to grow.

《Science》2011.2.25 第 331 卷 6020 期

内容精选

延伸阅读

内容精选

1. 随着转基因真菌的发展将可以杀死蚊群中人类的疟疾寄生虫

标题：Development of Transgenic Fungi That Kill Human Malaria Parasites in Mosquitoes

作者：Weiguo Fang, Joel Vega-Rodríguez, Anil K. Ghosh, Marcelo Jacobs-Lorena, Angray Kang, and Raymond J. St. Leger

来源出版物：Science 卷：331 期：6020 页：1074-1077 时间：25 February 2011

摘要：Metarhizium anisopliae infects mosquitoes through the cuticle and proliferates in the hemolymph. To allow M. anisopliae to combat malaria in mosquitoes with advanced malaria infections, we produced recombinant strains expressing molecules that target sporozoites as they travel through the hemolymph to the salivary glands. Eleven days after a Plasmodium-infected blood meal, mosquitoes were treated with M. anisopliae expressing salivary gland and midgut peptide 1 (SM1), which blocks attachment of sporozoites to salivary glands; a single-chain antibody that agglutinates sporozoites; or scorpine, which is an antimicrobial toxin. These reduced sporozoite counts by 71%, 85%, and 90%, respectively. M. anisopliae expressing scorpine and an [SM1]8:scorpine fusion protein reduced sporozoite counts by 98%, suggesting that Metarhizium-mediated inhibition of Plasmodium development could be a powerful weapon for combating malaria.

（用真菌抗击疟疾）研究人员说，用真菌来感染体内有疟原虫的蚊子可以是一种释放可控制疟疾扩散的毒素、抗体和其他制剂的有效方法。Weiguo Fang 及其同事将特殊的生物制剂基因置入到可感染蚊子的真菌（金龟子绿僵菌）之中，并发现某些基因的组合会终止疟原虫在蚊子体内的发育。他们说，这一通过接触并能像在户内和户外使用的化学物品那样的真菌给药系统可做基因修饰以对抗可能在演变中出现的抵抗力。就眼下而言，该真菌给药系统可有效地用于许多对杀虫剂有抵抗力的蚊子，这些有抵抗力的蚊

子会将疟原虫传播给人类宿主。Fang 及其同事制备了不同的会表达一种肽、一种抗体和一种抗微生物毒素（或具有所有 3 种物质的组合）的金龟子绿僵菌株，并将它们打造成针对感染蚊子体内的孢子体（孢子体是疟原虫所产生的可感染新宿主的细胞）的物质。一种蝎毒素加上一种唾液腺及中肠肽的特别组合在通过真菌释放出来后可将孢子体的计数减少 98%。这些发现表明，这种由金龟子绿僵菌所介导的对疟原虫的抑制最终可能成为对抗这种疾病的一种有价值的武器。

2. 新生哺乳动物的心脏在受损后能够自我愈合

标题：Transient Regenerative Potential of the Neonatal Mouse Heart

作者：Enzo R. Porrello, Ahmed I. Mahmoud, Emma Simpson, Joseph A. Hill, James A. Richardson, Eric N. Olson, and Hesham A. Sadek

来源出版物：Science 卷：331 期：6020 页：1078-1080 时间：25 February 2011

摘要：Certain fish and amphibians retain a robust capacity for cardiac regeneration throughout life, but the same is not true of the adult mammalian heart. Whether the capacity for cardiac regeneration is absent in mammals or whether it exists and is switched off early after birth has been unclear. We found that the hearts of 1-day-old neonatal mice can regenerate after partial surgical resection, but this capacity is lost by 7 days of age. This regenerative response in 1-day-old mice was characterized by cardiomyocyte proliferation with minimal hypertrophy or fibrosis, thereby distinguishing it from repair processes. Genetic fate mapping indicated that the majority of cardiomyocytes within the regenerated tissue originated from preexisting cardiomyocytes. Echocardiography performed 2 months after surgery revealed that the regenerated ventricular apex had normal systolic function. Thus, for a brief period after birth, the mammalian heart appears to have the capacity to regenerate.

（哺乳动物心脏再生的一个时间窗）研究人员报道说，在一个短暂的时段中，新生小鼠的心脏可在受到损伤之后自我重建。尽管这种再生的能力会在几天之后就消失，但这些发现提示，人类心脏也可能有着比原先所认为的更大的自我再生的潜力。蛙类、蝾螈及某些鱼类在受伤之后可重建它们的心肌，但这种情况则不存在于成年的哺乳动物之中。人们一直不清楚哺乳动物是否完全缺乏心肌再生的能力，或是这种能力是存在的，但却在出生之后立刻就停止了。Enzo Porrello 及其同事现在显示，将一天大的小鼠的部分心室手术切除可触发一种反应，该反应促使一个有功能且有正常解剖结构的心室的再生。在这一反应中包括了被称作心肌细胞的增生，但该反应会在小鼠出生 7 天后消失。如果研究人员能够找到这一再生反应的机制，并知道该机制是如何被关掉的，那么这一资讯可产生修补人类因疾病而受损的心脏的新方法。

3. 大肠杆菌中 mRNA的独立平移性定位

标题：Translation-Independent Localization of mRNA in E. coli

作者：Keren Nevo-Dinur, Anat Nussbaum-Shochat, Sigal Ben-Yehuda, and Orna Amster-Choder

来源出版物：Science 卷：331 期：6020 页：1081-1084 时间：25 February 2011

摘要：Understanding the organization of a bacterial cell requires the elucidation of the mechanisms by which proteins localize to particular subcellular sites. Thus far, such mechanisms have been suggested to rely on embedded features of the localized proteins. Here, we report that certain messenger RNAs (mRNAs) in Escherichia coli are targeted to the future destination of their encoded proteins, cytoplasm, poles, or inner membrane in a translation-independent manner. Cis-acting sequences within the transmembrane-coding sequence of the membrane proteins are necessary and sufficient for mRNA targeting to the membrane. In contrast to the view that transcription and translation are coupled in bacteria, our results show that, subsequent to their synthesis, certain mRNAs are capable of migrating to particular domains in the cell where their future protein products are required.

延伸阅读

新生哺乳动物心脏受损后能自愈

美国德州大学西南医学中心的研究人员在 2 月 25 日出版的《科学》杂志上报告说，老鼠实验表明，新生哺乳动物的心脏在受损后完全能够自我愈合，这一发现可为治疗人类心脏病提供新的思路。

实验中，研究人员将刚出生一周的小鼠 15%的心脏切除，结果发现，在 3 周内，受损的心脏重新完好地长出来，其外观和功能与正常心脏无异。研究人员认为，仍在跳动的未受损的心脏细胞，也就是心肌细胞，是新生细胞的主要来源。这些心肌细胞会停止跳动一段时间并且分裂，从而为心脏提供新鲜的心肌细胞。

“心脏病是发达国家威胁人们健康的头号杀手，这是我们在寻找心脏病治疗方法的道路上迈出的重要一步。”该研究报告作者之一、内科医学助理教授希沙姆•萨迪克说，“我们发现，新生哺乳动物的心脏能够自我修复，它只是在发育老化的过程中忘记了这一技能。目前的挑战是要找到一种方法来帮助成年后的心脏回想起如何重新进行自我修复。”

此前的研究已经证明，一些能够重新长出鳍和尾巴的鱼类和两栖类动物等低等生物也可以部分再生其受损的心脏。“相比之下，成年哺乳动物的心脏缺乏这种重新长出失去的或者受损的组织的能力，其结果是，当心脏出现损伤时，比如心脏病发作后，心脏就会变得越来越虚弱，最终导致心脏衰竭。”萨迪克说。

报告的另一位作者、分子生物学家埃里克•奥尔森博士说，成年后的心脏在发生损伤时无法再生，这是心血管医学领域面临的一个主要障碍。而这项工作表明，在出生后的一段“窗口期“内，哺乳动物的心肌再生是有可能的，只是这种再生能力随后就失去了。有了这些认识，未来将可以通过药物、基因或者其他方法以唤醒成年老鼠乃至成人的心肌再生能力。

研究人员表示，他们下一步将趁心脏仍具备再生能力时对这个短暂的“窗口期”加以研究，并找出心脏是如何以及为什么会在生长发育的过程中“关闭”这一非凡能力的答案。

作者： Enzo R. Porrello 等 来源：《科学》

http://paper.sciencenet.cn/htmlpaper/20112281428465115293.shtm

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