中国机构
CNS月报

05月报

生物探索出品

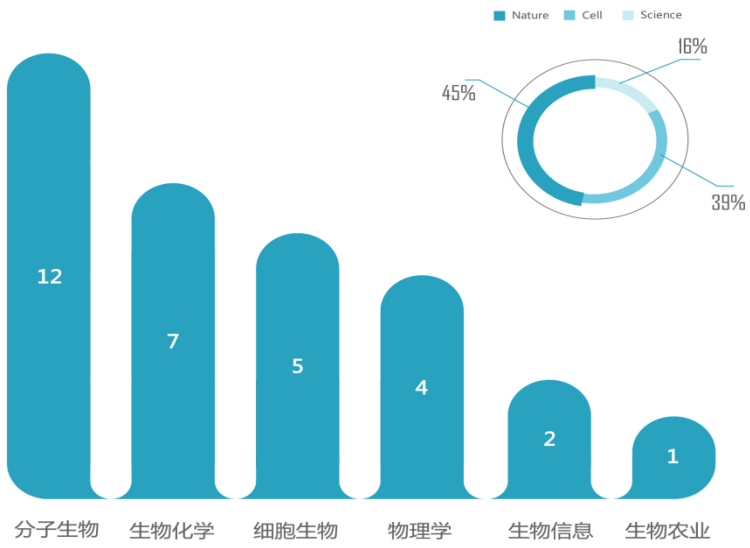
目　录

一、导语

令国内科研界振奋的是，自然系列期刊在 2012 年的论文统计显示，发文 140 篇论文的中国科学院超过日本东京大学排名亚洲机构第一位，这也是 Nature Index 统计以来中国科研机构首次排名第一，反映出中国顶尖科研机构在数量上领跑亚洲。据生物探索统计，2013 年 5 月份中国科研机构在 Nature、Cell 和 Science 三大系列期刊的总发文量是 31 篇，同比上升了 14.8%，而前 5 个月发文 179 篇，同比增长了 62.7%。

在生物学领域，三大期刊（Cell、Nature 和 Science）及其子刊，简称 CNS，倍受中国研究人员推崇，他们希望凭借 CNS 在学术界的威望将中国最尖端、最前沿的研究成果向全世界传达。这些研究动态可谓是中国科研机构的最高水平。作者希望对此进行统计，以便于从发文成果追踪国内科研经费动向，同时，生物医药圈内的研究人员和学生可实时了解中国顶尖研究人员从事研究的的领域和方向。

二、5 月份中国机构 CNS 发文与学术领域热度

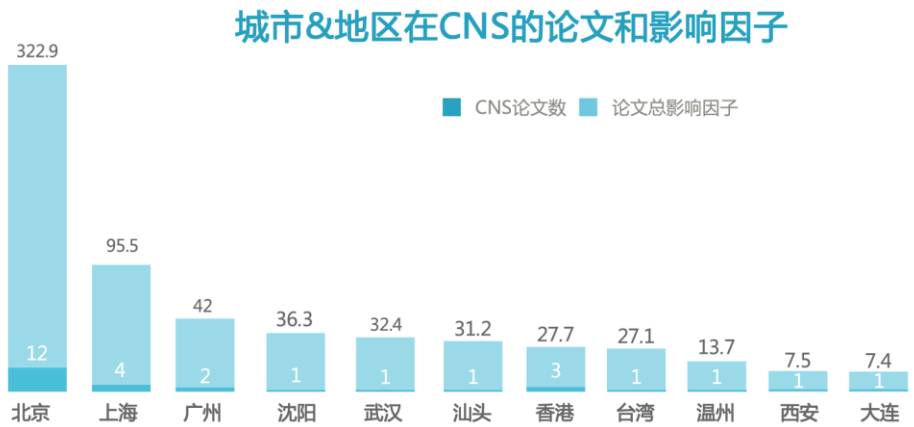


（饼状图表示期刊论文百分数）

2013 年 5 月份中国研究机构在三大系列期刊共发表 31 篇论文，包括 Nature 系列 14 篇、Cell 系列 12 篇和 Science 系列 5 篇，其中 Nature 主刊、Cell 主刊和 Science 主刊的发文量分别是 3 篇、5 篇和 4 篇。从数据上看，CNS 三大主刊中 Cell 主刊（5 篇）是发表中国机构论文的最多的，同时也改变了 3、4 月份未发表中国机构论文的纪录；发文中国机构论文一直处于上位的 Nature 系列期刊由 4 月份所占比例高于 80%下降到 5 月份 50%以下。从地区上看，5 月份发表 27 篇的大陆地区仍然是中国机构发表 CNS 论文的主体，而港台地区共发表 4 篇，这是近 4 个月内发文最多的。

5 月份 CNS 发表的中国机构研究论文中，分子生物领域（12 篇）排在第 1 位，而上月并列第一的生物化学领域排在第二位以及物理学领域排在第 4 位。从学术热度上看，以基因组学为对象的生物信息学研究持续成为热点，近 9 个月中国研究机构都有关于基因组测序的 CNS 论文发表，5 月份发表在 Nature Genetics 的 2 篇生物信息学论文分别讲到汉族人先天性心脏病的潜在致病位点以及食管鳞状细胞癌患者存活期相关的遗传位点。此外，在上图 6 个论文分类中，Cell 系列刊和 Science 系列刊分别占有 3 个和 2 个，而 Nature 系列刊却包括 6 个。

三、5 月份城市&地区在 CNS 的论文和影响因子



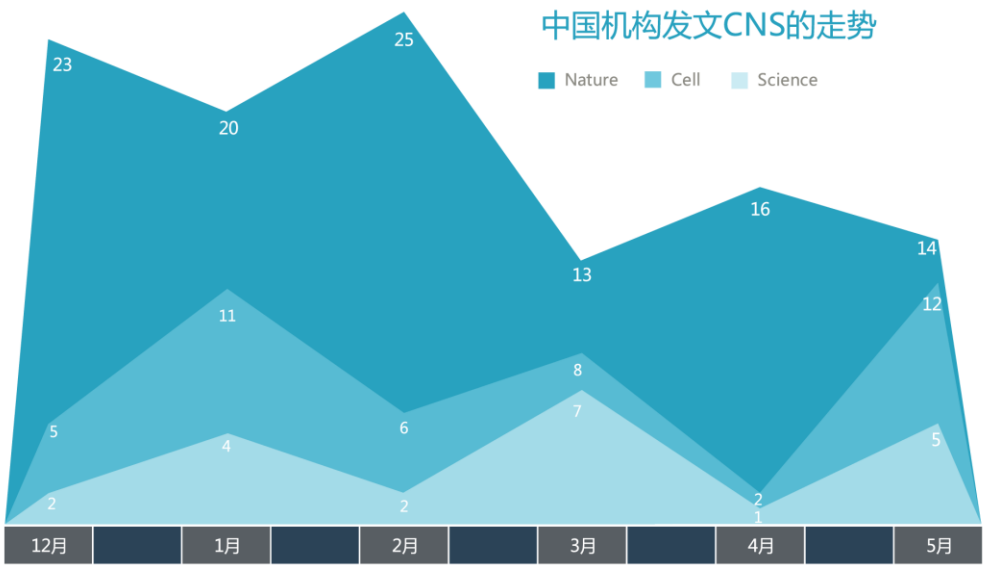
（影响因子源自 MedSci 查询系统，取小数点后一位）

从 CNS 论文影响因子看，5 月份超过 100 分的城市&地区仅有北京，它以 322.9 分（12 篇论文）卫冕排行榜，较上月上升了 116%，而发文 4 篇的上海获得了 95.9 分，其在 3、4 月份 CNS 影响因子都超过了 100 分。 从上图可以看出，北京的 CNS 论文影响因子遥遥领先其它城市&地区。

在 5 月份，除北京外其它城市发表的 CNS 论文数都不多，发表 1 篇论文以上的城市&地区是上海（4 篇）、香港（3 篇）和广州（2 篇），而仅发表 1 篇论文的城市&地区是沈阳、武汉、汕头、台湾、温州、西安和大连。

对城市&地区的 CNS 影响因子统计，生物探索网站希望向用户提供关于地区研究水平的一项指数，让科研人员在从事各自研究领域的同时选择较高的研究平台和学术氛围。此外，由于论文来自不同的经费项目，因此城市&地区的 CNS 影响因子能从一个方面反映国家经费的分配比例。

四、5 月份中国机构发文 CNS 的走势



（数据统计源自 NCBI 网站 Pubmed）

在 2012 年 12 月至 2013 年 5 月之间中国机构发文 CNS 的统计结果中，数据表明：Nature 及其子刊发表的中国研究论文数量处于高位，总计 111 篇，其中 2 月最高达到 25 篇；相反，Science 及其子刊发表的中国研究论文数量处于低位，总计 21 篇，其中 3 月最高达到 7 篇。

Nature 系列期刊的数量最多，它覆盖的学术类别和影响因子也较多，这是中国研究论文发表在 Nature 系列刊最多的原因之一；另一原因可能是，Nature 系列期刊对中国机构的研究成果认可度高，从自然出版集团在上海设立《自然-通讯》编辑部一事可以看出，它对中国机构研究成果的重视。

五、5 月份 CNS 发文机构论文量统计

研究机构	CNS 论文		
	5 月份发文量	近 5 年总数	总数
中国科学院上海生命科学研究院	2	68	96
清华大学	2	67	82
北京大学	2	42	51
复旦大学	1	35	43
香港科技大学	1	25	40
上海交通大学	3	33	37
中国科学院生物物理研究所	1	24	36
中国医学科学院（北京协和医学院）	1	21	24
中国科学院遗传与发育生物学研究所	1	17	20
中国农业大学	1	12	18
武汉大学	1	12	15
中国科学院金属研究所	1	7	11
中国农业科学院	1	9	9
中国科学院广州生物医药与健康研究院	1	7	7
北京师范大学	2	7	7
中国科学院大学	1	7	7
南京中医药大学	1	6	6
中国科学院微生物研究所	1	6	6
西安交通大学	1	6	6
国立交通大学	1	5	6
香港城市大学	1	2	6
中国科学院北京基因组研究所	1	3	4
大连理工大学	1	3	3
汕头大学	1	1	3
中科院上海生命科学院/上海交通大学医学院健康科学研究所	1	2	2
温州医科大学	1	1	1
南方医科大学	1	1	1

（数据源于NCBI网站Pubmed）

从 5 月份中国机构 CNS 论文榜单上看，排名前三的分别中国科学院上海生命科学研究院、清华大学和北京大学。在本月发文量上，超过 1 篇的研究机构是上海交通大学（3 篇）、中国科学院上海生命科学研究院（2 篇）、清华大学（2 篇）、北京大学（2 篇）和北京师范大学（2 篇）。其中发文 3 篇的上海交通大学是中国机构 5 月 CNS 发文最多的研究机构，而前两个月清华大学都以 4 篇论文量成为当月发文最多的研究机构。

在 5 月份 CNS 论文的统计数据中，除香港城市大学和汕头大学以外，中国机构近 5 年发表的 CNS 论文总数不低于其 CNS 论文总数的一半，这表明近 5 年来中国机构发文 CNS 的速度和数量增加较快。5 月份，温州医科大学和南方医科大学都是首次发文 CNS，除首次发文 CNS 的研究机构外，中国农业科学院、中国科学院广州生物医药与健康研究院、北京师范大学、中国科学院大学、南京中医药大学、中国科学院微生物研究所、西安交通大学、大连理工大学和中科院上海生命科学院/上海交通大学医学院健康科学研究所的 CNS 论文全都在近 5 年内。

六、5 月份 CNS 论文通讯作者的项目数和经费

研究机构	通讯作者	项目金额/万	项目数/个
中国农业大学	张福锁	2130.7	23
中国科学院微生物研究所	高福	1345.4	15
中国科学院金属研究所	成会明	1238.7	20
上海交通大学医学院	陈竺	1082.6	20
中国科学院遗传与发育生物学研究所	傅向东	952.8	8
中国医学科学院	林东昕	699	8
南京中医药大学	沈洪兵	664.5	7
清华大学	谢道昕	662	4
北京大学	俞大鹏	659	12
中国科学院广州生物医药与健康研究院	裴端卿	624.6	6
南方医科大学	高天明	610.4	11
中科院上海生命科学院/上海交通大学医学院健康科学研究所	钱友存	572	4
北京大学	邓宏魁	508	6
上海交通大学医学院	房静远	427	5
北京师范大学	贾宗超	360	2
北京师范大学	邱小波	280	2

中国农业科学院	陈化兰	262	3
南京中医药大学	胡志斌	255	3
中国人民解放军第四军医大学	招明高	191	4
中国科学院生物物理研究所	王大成	156.7	7
中国科学院北京基因组研究所/中国科学院大学	慈维敏	150	2
北京大学	廖志敏	111.5	3
南京中医药大学	周作民	109	3
南方医科大学	朱心红	106	3
大连理工大学	董星龙	103.4	3
中国科学院上海生命科学研究院	王佳伟	100	1
复旦大学	王文宁	97	4
南京中医药大学	陈亦江	77	2
北京大学	汤超	40	1
中国科学院生物物理研究所	丁璟珒	25	1
温州医科大学	李校堃	8	3

（数据源于 NSFC）

对于 5 月份中国机构发文 CNS 的 31 位通讯作者（统计量不完全），国家自然科学基金项目提供了详细的项目金额和数量。中国农业大学的张福锁教授以 2130.7 万元高举榜首，项目数为 23 个；中国科学院微生物研究所的高福研究员和中国科学院金属研究所的成会明研究员以 1345.4 万和 1238.7 万分列第二、三名，他们的项目数为 15 和 20 个。

排名前 10 的通讯作者分别来自北京（6 位）、上海（1 位）、南京（1 位）、沈阳（1 位）和广州（1 位）。其中，北京地区 6 位通讯作者位于项目金额榜前十位之内，这反映出北京位列 5 月份 CNS 中国机构影响因子之首的经费基础。

七、受关注的权威看法

沈保根院士：将科研人员从挣钱中解放出来

对大多数科研人员来说，他们往往需要同时承担多个研究项目才能满足工作需要，有的资助还断断续续，影响了工作的连续性。”中科院院士沈保根接受采访时说，为何科研投入越来越大，原创性成果却没有正比上升？科研经费分配制度不够完善是原因之一。

近年来，国家对科研的投入越来越多，科研经费大幅增长。2012 年，全社会用于研发活动的支出达 10240 亿元，占 GDP 的 1.97%，科研经费占 GDP 比重已达中等发达国家水平。同时有统计结果表明，我国论文总数已连续多年位列全球第二，仅次于美国。

然而，沈保根认为，“我国科研经费的分配已形成了多渠道投入的格局，各部门资助基本上独立运作，使少数同一研究内容的申请可以从多个渠道得到重大资助，进而产生不必要的浪费”。

沈保根所说的情况的确比较普遍。当前科研人员经常一个人同时承担着 4～5 个项目，有的甚至承担 7～8 个项目，但每一个项目所得到的资助却又十分有限。

这导致的后果是许多科研人员不得不把主要精力放在申请科研经费、应付各种检查总结汇报等方面，其真正安下心来作研究的时间明显不足，甚至“有些工作只是为了交账，而较少考虑集中精力作深入系统的研究”。

因此，“有的导师进实验室的次数越来越少，把实验工作基本上交给学生。导师忙于挣钱，学生埋头干活，经常有学生把自己的导师称为‘老板’”。

沈保根觉得，国家应大幅提高基础研究项目的单项资助强度，减少科研人员申请项目的次数。让基金管理工作人员从应付大量申请和评审工作中解放出来，将更多的精力放在质量管理上，也让一线科研人员减少花在项目评审上的时间。

他建议，把更多的经费用于安排自由申请的面上项目。“对重大研究项目不宜设立针对性很强的申请指南，允许更多同行参与合理竞争。对非常优秀的人才和特别优秀的项目继续给予特别支持，但也要避免科研经费的过分集中。”

此外，沈保根还呼吁国家要特别重视培养 35 岁以下的年轻科技人才。“一般教授和研究员花较多时间和精力还是能够申请到科研经费，但年轻科技人员作为负责人申请到经费还是有不少难度。现在虽然有针对年轻人的项目，但数量还远远不够，每项资助的强度又相对较低，在一定程度上影响了年轻科研人员创造性的发挥。”

“年轻人才的成长是国家未来发展的希望。国家不仅要让年轻科技人员有更多渠道申请研究经费，而且尽可能要使每位优秀年轻人才都能获得较强的资助机会。”他说。

科技部部长万钢：管好用好科研经费是科技界共同责任和义务

科技部、财政部共同召开“加强科技计划经费监管暨启动科技部 2013 年科研经费巡视检查工作会议”。全国政协副主席、科技部部长万钢出席会议并讲话。他指出，财政科研经费是公共财富，是纳税人的钱，管好用好，切实保障资金的安全，发挥出资金的效益，是科技管理部门的职责所在，也是每个科研单位、承担科技项目的科技人员的责任和义务。

据悉，“十一五”以来，科技部对执行过程中的近 3000 个课题开展了专项审计，共涉及财政资金 433.87 亿元，经费覆盖率达 70%；对全部 10400 个结题课题都进行了结题财务审计和财务验收，设计财政资金 992 亿元，覆盖率达 100%；对江苏、重庆、贵州、陕西、山东、陕西等 12 个省（区、市）90 多个单位、160 多个项目开展了巡视检查。今年 6—9 月，科技部将抽选承担国家科技计划项目（课题）较多、科技经费数额较大，以及此前未及时整改到位和被举报且具有明显检查线索的多家项目（课题）承担单位，派巡视组择机开展现场巡视检查。

万钢在讲话中表示，科技部将把科研人员作为开展监管工作的根本出发点和立足点，寓监管于服务之中。通过加强宣传培训力度，为科研人员答疑解惑，让科研单位和科研人员熟悉政策、理解规定、正确运用。其次，科技经费监管工作要紧紧依靠承担科技项目的法人单位。课题承担单位对课题的经费使用要行使监督权，要有切实的内控监督制度，使国家财政资金的管理要求在本单位落到实处，确保资金的合理使用和安全。同时，各单位也要切实落实科研人员的激励政策。要对经费相对比较集中的重点科研团队，配备财务管理人员专门管理经费，使科学家能够集中精力投身科研。第三，作为科技项目过程管理的一个重要环节，科研经费巡视检查工作是要依据规章制度，对经费使用过程进行检查，对一些重大项目、重点课题要重点抽查。对于违规现象要制止整改，对于违纪违法的情况要零容忍，一旦发现查实，要知会法人单位，依法依规进行处理。他强调，保证财政科技资金安全，提高资金使用效益，要靠管理部门加强监督检查和主动服务，帮助科研单位和科研人员发现问题、解决问题，更要靠科研工作者廉洁自律，自觉作为。

八、专家精选

Infectivity, Transmission, and Pathology of Human H7N9 Influenza in Ferrets and Pigs.（汕头大学&香港大学）

任职于香港大学和汕头大学的管轶教授联合其它研究小组，与中国疾病预防控制中心国家流感中心合作，发现引发内地多宗人类感染个案的甲型禽流感 H7N9 病毒，不仅可以感染与人类受病毒感染和传播情况相近的雪貂，并引发出与 2009 年新甲型流感 H1N1 病毒类似的病症，

而且病毒可以通过密切接触有效地在雪貂个体间传播，并可以出现有限度的空气飞沫传播。研究同时发现 H7N9 病毒可以感染猪只，引起呼吸道感染和轻度肺炎。研究结果不排除此病毒进化后，有引起流感大爆发的可能。相关研究成果发表在《科学》（Science）期刊上。

研究人员利用与人类感染和传播情况相近的雪貂进行动物实验，发现感染了 H7N9 病毒的雪貂在 24 小时内开始出现较高病毒载量的排毒，随后出现发热、喷嚏、流涕、倦怠、咳嗽、肺炎等症状。感染动物的排毒期为 5 至 7 天。在感染后第 7 天，动物体内开始出现特异性抗体，同时肺部及其他器官的病毒也逐渐被清除。感染第 14 至 16 天后，雪貂基本健康恢复正常。总体上看, H7N9 病毒的感染性和临床表现与 2009 年新甲型流感 H1N1 病毒相近。

自今年 3 月份以来，中国内地已经确诊了 131 宗人类感染甲型禽流感 H7N9 病毒的个案。当中在上海、山东的家庭聚集性病例，引起了公众对 H7N9 病毒人传人的忧虑。

Structural biology: tiny enzyme uses context to succeed.（北京师范大学）

北京师范大学的郑积敏教授和贾宗超教授（左图）对大肠杆菌中甘油二酯激酶的晶体结构进行了深入的分析，揭示了这种镶嵌在细胞膜上的激酶是如何利用其残基在 细胞膜附近的环境中完成其功能使命的，这将有助于我们从整体上理解完整的细胞膜激酶的活性机制。相关研究发表在《自然》（Nature）期刊上。

研 究人员成功解析了存在于大肠杆菌细胞内膜中的甘油二酯激酶的晶体结构（大小仅为 121 个氨基酸残基，并从中发现了这种酶如何利用其残基附近环境的奥秘—— 酶中每个单体都“借用”了“邻居”的组成成分，构成组成性活性位点。这种借来的元件同时具有亲水性和疏水性的氨基酸末端螺旋，能定位在膜和胞质之间界面 上，组成了一个关键的催化残基。此外，这种晶体结构与以前通过核磁共振（NMR）获得的甘油二酯激酶“只有骨架”的结构并不相同，虽然甘油二酯激酶整体三 聚体结构是一致的，但是活性位点却存在巨大的差别。

甘油二酯激酶巧妙设计了它的活性位点，这比其它种类的激酶都要简单。值得肯定的是，甘油二酯激酶结构解析将会为膜蛋白的相关催化机制和构架提出新的研究方向，未来科学家们可以进一步解析这种酶的催化机制，以及调控机理，并深入探讨 NMR 方 法和晶体结构方法

之间的分辨率差异。

Genome-wide association study identifies common variants in SLC39A6 associated with length of survival in esophageal squamous-cell carcinoma.（中国医学科学院北京协和医学院）

中国医学科学院北京协和医学院的林东昕教授，利用全基因组关联方法（GWAS）确定了一个与食管鳞状细胞癌生存期相关的基因 SLC39A6，这些研究推动了对食管癌发生发展机制的认识，并为该类型肿瘤提供一个潜在的治疗靶点。相关研究成果发表在《自然 遗传学》（Nature Genetics）杂志上。

为了研究食管鳞状细胞癌患者生存预后相关的遗传因素，研究人员首先对 1331 个食管鳞状细胞癌患者的基因组 DNA 进行了全基因组分析，然后对发现的相关 SNPs 在两个独立样本共 1962 名食管鳞状细胞癌患者中进行了验证。确定了 SLC39A6 的 rs1050631 与受累个体的生存时间相关，综合样本的食管鳞状细胞癌的死亡危险比率为 1.30。

此外，研究人员鉴定出了与食管鳞状细胞癌预后相关的新遗传区域 rs7242481，其定位于 SLC39A6 5’ UTR 区域内，因破坏了该区域与转录抑制因子结合而导致 SLC39A6 高表达。采用免疫组化染色食管鳞状细胞癌组织，研究人员证实 SLC39A6 高表达与晚期食管鳞状细胞癌患者生存期缩短有关。而下调 SLC39A6 表达，则可抑制食管鳞状细胞癌细胞的增殖与侵袭力。

An Increase in Synaptic NMDA Receptors in the Insular Cortex Contributes to Neuropathic Pain.（中国人民解放军第四军医大学&西安交通大学）

中国人民解放军第四军医大学的招明高教授联合其它研究机构在新研究中揭示了神经性疼痛的分子根源，证实疼痛是由于大脑岛叶皮质中突触 NMDA 受体增加所导致。从而为推动开发出有潜力的靶向疗法指明了新方向。相关研究成果发表《科学信号》（Science Signaling）期刊上。

研究人员利用小鼠模型证实周围神经损伤可导致神经性疼痛发生，岛叶皮质突触可塑性发生改变，其与突触 N- 甲基-D- 天氡氨酸受体数量长期升高有关，但与突触外 NMDARs 数量无

关。此外，激活环腺苷酸（cAMP）依赖性信号通路，可以提高急性分离岛叶皮质切片中的突触 NMDARs 数量，促进培养皮质神经元中 NMDARs 细胞表面定位。经证实，通过 AC1（腺苷酸环化酶亚型 1)/ PKA(蛋白激酶 A)/ SFK(Src 家族激酶)信号通路磷酸化 NMDAR 亚基 GluN2B，其是 NMDARs 数量增高的必要条件。当他们将 NMDAR 或 GluN2B 特异性拮抗剂注入到岛叶皮质中时，证实可以降低神经性疼痛小鼠模型对于正常非伤害性(nonnoxious)刺激的行为反应。

神经性疼痛是一种神经系统原发损害或功能障碍引起的慢性疼痛疾病，而神经性疼痛一直是困扰医学界的难题。这项研究表明，神经损伤可引起岛叶皮质突触 NMDA 受体增加，导致出现活动依赖性可塑性，从而引发了神经性疼痛发生。抑制 NMDAR 功能将有助于预防或治疗神经性疼痛。

九、5 月份论文列表

1、Nature 及其子刊

A panoramic view of acute myeloid leukemia. [链接]

通讯作者：陈竺（上海交通大学医学院）Nat Genet. 2013 May 29;45(6):586-7.

A recent study in the New England Journal of Medicine reports the genomic and epigenomic changes in adult acute myeloid leukemia (AML). The patterns of somatic mutation suggest biologically relevant connections between the functional categories of genes driving AML.

Catalytically active single-atom niobium in graphitic layers. [链接]

通讯作者：董星龙（大连理工大学）Nat Commun. 2013 May 28;4:1924. doi: 10.1038/ncomms2929.

Carbides of groups IV through VI (Ti, V and Cr groups) have long been proposed as substitutes for noble metal-based electrocatalysts in polymer electrolyte fuel cells. However, their catalytic activity has been extremely limited because of the low density and stability of catalytically active sites. Here we report the excellent performance of a niobium-carbon structure for catalysing the cathodic oxygen reduction reaction. A large number of single niobium atoms and ultra small clusters trapped in graphitic layers are directly identified using state-of-the-art aberration-corrected scanning transmission electron microscopy. This structure not only enhances the overall conductivity for accelerating the exchange of ions and electrons, but it suppresses the chemical/thermal coarsening of the active particles. Experimental results coupled with theory

calculations reveal that the single niobium atoms incorporated within the graphitic layers produce a redistribution of d-band electrons and become surprisingly active for O2 adsorption and dissociation, and also exhibit high stability.

Layer-by-layer assembly of vertically conducting graphene devices. [链接]

通讯作者：廖志敏 俞大鹏（北京大学）Nat Commun. 2013 May 28;4:1921. doi: 10.1038/ncomms2935.

Graphene has various potential applications owing to its unique electronic, optical, mechanical and chemical properties, which are primarily based on its two-dimensional nature. Graphene-based vertical devices can extend the investigations and potential applications range to three dimensions, while interfacial properties are crucial for the function and performance of such graphene vertical devices. Here we report a general method to construct graphene vertical devices with controllable functions via choosing different interfaces between graphene and other materials. Two types of vertically conducting devices are demonstrated: graphene stacks sandwiched between two Au micro-strips, and between two Co layers. The Au|graphene|Au junctions exhibit large magnetoresistance with ratios up to 400% at room temperature, which have potential applications in magnetic field sensors. The Co|graphene|Co junctions display a robust spin valve effect at room temperature. The layer-by-layer assembly of graphene offers a new route for graphene vertical structures.

A genome-wide association study identifies two risk loci for congenital heart malformations in Han Chinese populations. [链接]

通讯作者：沈洪兵 陈亦江 周作民 胡志斌 （南京中医药大学）Nat Genet. 2013 May 26. doi: 10.1038/ng.2636.

Congenital heart malformation (CHM) is the most common form of congenital human birth anomaly and is the leading cause of infant mortality. Although some causative genes have been identified, little progress has been made in identifying genes in which low-penetrance susceptibility variants occur in the majority of sporadic CHM cases. To identify common genetic variants associated with sporadic non-syndromic CHM in Han Chinese populations, we performed a multistage genome-wide association study (GWAS) in a total of 4,225 CHM cases and 5,112 non-CHM controls. The GWAS stage included 945 cases and 1,246 controls and was followed by 2-stage validation with 2,160 cases and 3,866 controls. The combined analyses identified significant associations ($P < 5.0 \times 10^{-8}$) at 1p12 (rs2474937 near TBX15; odds ratio (OR) = 1.40; $P = 8.44 \times 10^{-10}$) and 4q31.1 (rs1531070 in MAML3; OR = 1.40; $P = 4.99 \times 10^{-12}$). These results extend current knowledge of genetic contributions to CHM in Han Chinese populations.

Sequential introduction of reprogramming factors reveals a time-sensitive requirement for individual factors and a sequential EMT-MET mechanism for optimal reprogramming. [链接]

通讯作者：裴端卿 郑辉（中国科学院广州生物医药与健康研究院）Nat Cell Biol. 2013 May 26. doi: 10.1038/ncb2765.

Present practices for reprogramming somatic cells to induced pluripotent stem cells involve simultaneous introduction of reprogramming factors. Here we report that a sequential introduction protocol (Oct4-Klf4 first, then c-Myc and finally Sox2) outperforms the simultaneous one. Surprisingly, the sequential protocol activates an early epithelial-to-mesenchymal transition (EMT) as indicated by the upregulation of Slug and N-cadherin followed by a delayed mesenchymal-to-epithelial transition (MET). An early EMT induced by 1.5-day TGF-β treatment enhances reprogramming with the simultaneous protocol, whereas 12-day treatment blocks reprogramming. Consistent results were obtained when the TGF-β antagonist Repsox was applied in the sequential protocol. These results reveal a time-sensitive role of individual factors for optimal reprogramming and a sequential EMT-MET mechanism at the start of reprogramming. Our studies provide a rationale for further optimizing reprogramming, and introduce the concept of a sequential EMT-MET mechanism for cell fate decision that should be investigated further in other systems, both in vitro and in vivo.

Materials science: when two is better than one. [链接]

通讯作者：成会明（中国科学院金属研究所）Nature. 2013 May 23;497(7450):448-9. doi: 10.1038/497448a.

Aerogels have many potential applications but usually suffer from poor elasticity. The synergistic assembly of carbon nanotubes and graphene has now allowed multifunctional, ultra-lightweight and super-elastic aerogels to be made.

A transparent electrode based on a metal nanotrough network. [链接]

通讯作者：Yi Cui（清华大学）Nat Nanotechnol. 2013 May 19;8(6):421-5. doi: 10.1038/nnano.2013.84.

Transparent conducting electrodes are essential components for numerous flexible optoelectronic devices, including touch screens and interactive electronics. Thin films of indium tin oxide-the prototypical transparent electrode material-demonstrate excellent electronic performances, but film brittleness, low infrared transmittance and low abundance limit suitability for certain industrial applications. Alternatives to indium tin oxide have recently been reported and include conducting polymers, carbon nanotubes and graphene. However, although flexibility is greatly improved, the optoelectronic performance of these carbon-based materials is limited by low conductivity. Other examples include metal nanowire-based electrodes, which can achieve sheet resistances of less than 10Ω □(-1) at 90% transmission because of the high conductivity of the metals. To achieve these performances, however, metal nanowires must be defect-free, have conductivities close to their values in bulk, be as long as possible to minimize the number of wire-to-wire junctions, and exhibit small junction resistance. Here, we present a facile fabrication process that allows us to satisfy all these requirements and fabricate a new kind of transparent

conducting electrode that exhibits both superior optoelectronic performances (sheet resistance of ~2Ω □(-1) at 90% transmission) and remarkable mechanical flexibility under both stretching and bending stresses. The electrode is composed of a free-standing metallic nanotrough network and is produced with a process involving electrospinning and metal deposition. We demonstrate the practical suitability of our transparent conducting electrode by fabricating a flexible touch-screen device and a transparent conducting tape.

Structural biology: tiny enzyme uses context to succeed.[链接]

通讯作者：贾宗超教授（北京师范大学）Nature. 2013 May 23;497(7450):445-6. doi: 10.1038/nature12245.

How the enzyme diacylglycerol kinase can form membrane anchors and an active site from so few amino-acid residues has long been a mystery. Crystal structures reveal that it gets by with a little help from its friends.

Peli1 sets the CNS on fire. [链接]

通讯作者：钱友存（中科院上海生命科学院/上海交通大学医学院健康科学研究所）Nat Med. 2013 May;19(5):536-8. doi: 10.1038/nm.3176.

It has long been unknown how activation of resident macrophages in the brain, or microglia, is regulated during the inflammatory pathogenesis of multiple sclerosis. Work in a mouse model of human multiple sclerosis identifies the E3 ubiquitin ligase Peli1 as a new crucial regulator of microglia activation.

DNA sequencing using electrical conductance measurements of a DNA polymerase. [链接]

通讯作者：G. Steven Huang（国立交通大学）Nat Nanotechnol. 2013 May 5;8(6):452-8. doi: 10.1038/nnano.2013.71. Epub 2013 May 5.

The development of personalized medicine-in which medical treatment is customized to an individual on the basis of genetic information-requires techniques that can sequence DNA quickly and cheaply. Single-molecule sequencing technologies, such as nanopores, can potentially be used to sequence long strands of DNA without labels or amplification, but a viable technique has yet to be established. Here, we show that single DNA molecules can be sequenced by monitoring the electrical conductance of a phi29 DNA polymerase as it incorporates unlabelled nucleotides into a template strand of DNA. The conductance of the polymerase is measured by attaching it to a protein transistor that consists of an antibody molecule (immunoglobulin G) bound to two gold nanoparticles, which are in turn connected to source and drain electrodes. The electrical conductance of the DNA polymerase exhibits well-separated plateaux that are ~3 pA in height. Each plateau corresponds to an individual base and is formed at a rate of ~22 nucleotides per second. Additional spikes appear on top of the plateaux and can be used to discriminate between the four different nucleotides. We also show that the sequencing platform works with a variety of

DNA polymerases and can sequence difficult templates such as homopolymers.

Astrocyte-derived ATP modulates depressive-like behaviors. [链接]

通讯作者：高天明 朱心红（南方医科大学）Nat Med. 2013 Jun;19(6):773-7. doi: 10.1038/nm.3162. Epub 2013 May 5.

Major depressive disorder (MDD) is a cause of disability that affects approximately 16% of the world's population; however, little is known regarding the underlying biology of this disorder. Animal studies, postmortem brain analyses and imaging studies of patients with depression have implicated glial dysfunction in MDD pathophysiology. However, the molecular mechanisms through which astrocytes modulate depressive behaviors are largely uncharacterized. Here, we identified ATP as a key factor involved in astrocytic modulation of depressive-like behavior in adult mice. We observed low ATP abundance in the brains of mice that were susceptible to chronic social defeat. Furthermore, we found that the administration of ATP induced a rapid antidepressant-like effect in these mice. Both a lack of inositol 1,4,5-trisphosphate receptor type 2 and transgenic blockage of vesicular gliotransmission induced deficiencies in astrocytic ATP release, causing depressive-like behaviors that could be rescued via the administration of ATP. Using transgenic mice that express a Gq G protein-coupled receptor only in astrocytes to enable selective activation of astrocytic Ca(2+) signaling, we found that stimulating endogenous ATP release from astrocytes induced antidepressant-like effects in mouse models of depression. Moreover, we found that P2X2 receptors in the medial prefrontal cortex mediated the antidepressant-like effects of ATP. These results highlight astrocytic ATP release as a biological mechanism of MDD.

Genome-wide association study identifies common variants in SLC39A6 associated with length of survival in esophageal squamous-cell carcinoma. [链接]

通讯作者：林东昕（中国医学科学院北京协和医学院）Nat Genet. 2013 May 5;45(6):632-8. doi: 10.1038/ng.2638. Epub 2013 May 5.

We conducted a genome-wide scan of SNPs to identify variants associated with length of survival in 1,331 individuals with esophageal squamous-cell carcinoma (ESCC), with associations validated in 2 independent sets including 1,962 individuals with this cancer. We identified rs1050631 in SLC39A6 as associated with the survival times of affected individuals, with the hazard ratio for death from ESCC in the combined sample being 1.30 (95% confidence interval (CI) = 1.19-1.43; P = 3.77 × 10(-8)). rs7242481, located in the 5' UTR of SLC39A6, disturbs a transcriptional repressor binding site and results in upregulation of SLC39A6 expression. Immunohistochemical staining of ESCC tissues showed that higher expression of SLC39A6 protein was correlated with shorter length of survival in individuals with advanced ESCC (P = 0.013). Knockdown of SLC39A6 expression suppressed proliferation and invasion in ESCC cells. These results suggest that SLC39A6 has an important role in the prognosis of ESCC and may be a potential therapeutic target.

Chinese agriculture: An experiment for the world. [链接]

通讯作者：张福锁（中国农业大学）Nature. 2013 May 2;497(7447):33-5. doi: 10.1038/497033a. No abstract available.

China's scientists are using a variety of approaches to boost crop yields and limit environmental damage, say Fusuo Zhang, Xinping Chen and Peter Vitousek.

Breaking news: thinking may be bad for DNA. [链接]

通讯作者：Jiali Li（香港科技大学） Nat Neurosci. 2013 May;16(5):518-9.

A study in this issue suggests that neuronal DNA double-strand breaks can result from natural behaviors. The breaks occur in the circuits that are activated and are enhanced in a model of Alzheimer's disease. The implications of this finding are far-reaching.

2、Cell 及其子刊

A comprehensive wiring diagram of the protocerebral bridge for visual information processing in the Drosophila brain. [链接]

通讯作者：Ann-Shyn Chiang（国立清华大学）Cell Rep. 2013 May 30;3(5):1739-53. doi: 10.1016/j.celrep.2013.04.022. Epub 2013 May 23.

How the brain perceives sensory information and generates meaningful behavior depends critically on its underlying circuitry. The protocerebral bridge (PB) is a major part of the insect central complex (CX), a premotor center that may be analogous to the human basal ganglia. Here, by deconstructing hundreds of PB single neurons and reconstructing them into a common three-dimensional framework, we have constructed a comprehensive map of PB circuits with labeled polarity and predicted directions of information flow. Our analysis reveals a highly ordered information processing system that involves directed information flow among CX subunits through 194 distinct PB neuron types. Circuitry properties such as mirroring, convergence, divergence, tiling, reverberation, and parallel signal propagation were observed; their functional and evolutional significance is discussed. This layout of PB neuronal circuitry may provide guidelines for further investigations on transformation of sensory (e.g., visual) input into locomotor commands in fly brains.

JAV1 Controls Jasmonate-Regulated Plant Defense. [链接]

通讯作者：谢道昕 （清华大学）Mol Cell. 2013 May 23;50(4):504-15.

Plants evolve effective mechanisms to protect themselves from environmental stresses and employ

jasmonates as vital defense signals to defend against insect attack and pathogen infection. Jasmonates are also recognized as an essential growth regulator by which diverse developmental processes are mediated. Despite substantial research, there are no key signaling components reported yet to control jasmonate-regulated plant defense independent of developmental responses. We identify JAV1, a key gene in the jasmonate pathway, which functions as a negative regulator to control plant defense but does not play a detectable role in plant development. Our results suggest that when encountering insect attack and pathogen infection, plants accumulate jasmonates that trigger JAV1 degradation via the 26S proteasome to activate defensive gene expression and elevate resistances against both insects and pathogens. These findings have provided insight into the molecular mechanism by which plants integrate jasmonate signals to protect themselves from insect attack and pathogen infection.

Acetylation-Mediated Proteasomal Degradation of Core Histones during DNA Repair and Spermatogenesis. [链接]

通讯作者：邱小波（北京师范大学） Cell. 2013 May 23;153(5):1012-24. doi: 10.1016/j.cell.2013.04.032.

Histone acetylation plays critical roles in chromatin remodeling, DNA repair, and epigenetic regulation of gene expression, but the underlying mechanisms are unclear. Proteasomes usually catalyze ATP- and polyubiquitin-dependent proteolysis. Here, we show that the proteasomes containing the activator PA200 catalyze the polyubiquitin-independent degradation of histones. Most proteasomes in mammalian testes ("spermatoproteasomes") contain a spermatid/sperm-specific α subunit α4 s/PSMA8 and/or the catalytic β subunits of immunoproteasomes in addition to PA200. Deletion of PA200 in mice abolishes acetylation-dependent degradation of somatic core histones during DNA double-strand breaks and delays core histone disappearance in elongated spermatids. Purified PA200 greatly promotes ATP-independent proteasomal degradation of the acetylated core histones, but not polyubiquitinated proteins. Furthermore, acetylation on histones is required for their binding to the bromodomain-like regions in PA200 and its yeast ortholog, Blm10. Thus, PA200/Blm10 specifically targets the core histones for acetylation-mediated degradation by proteasomes, providing mechanisms by which acetylation regulates histone degradation, DNA repair, and spermatogenesis.

Induction of pluripotency in mouse somatic cells with lineage specifiers. [链接]

通讯作者：邓宏魁 汤超（北京大学） Cell. 2013 May 23;153(5):963-75. doi: 10.1016/j.cell.2013.05.001.

The reprogramming factors that induce pluripotency have been identified primarily from embryonic stem cell (ESC)-enriched, pluripotency-associated factors. Here, we report that, during mouse somatic cell reprogramming, pluripotency can be induced with lineage specifiers that are pluripotency rivals to suppress ESC identity, most of which are not enriched in ESCs. We found that OCT4 and SOX2, the core regulators of pluripotency, can be replaced by lineage specifiers

that are involved in mesendodermal (ME) specification and in ectodermal (ECT) specification, respectively. OCT4 and its substitutes attenuated the elevated expression of a group of ECT genes, whereas SOX2 and its substitutes curtailed a group of ME genes during reprogramming. Surprisingly, the two counteracting lineage specifiers can synergistically induce pluripotency in the absence of both OCT4 and SOX2. Our study suggests a "seesaw model" in which a balance that is established using pluripotency factors and/or counteracting lineage specifiers can facilitate reprogramming.

Recent advances in microarray technologies for proteomics. [链接]

通讯作者：Shao Q. Yao（香港城市大学深圳研究院）Chem Biol. 2013 May 23;20(5):685-99. doi:10.1016/j.chembiol.2013.04.009.

Proteins are fundamental components of all living systems and critical drivers of biological functions. The large-scale study of proteins, their structures and functions, is defined as proteomics. This systems-wide analysis leads to a more comprehensive view of the intricate signaling transduction pathways that proteins engage in and improves the overall understanding of the complex processes supporting the living systems. Over the last two decades, the development of high-throughput analytical tools, such as microarray technologies, capable of rapidly analyzing thousands of protein-functioning and protein-interacting events, has fueled the growth of this important field. Herein, we review the most recent advancements in microarray technologies, with a special focus on peptide microarray, small molecule microarray, and protein microarray. These technologies have become prominent players in proteomics and have made significant changes to the landscape of life science and biomedical research. We will elaborate on their performance, advantages, challenges, and future directions.

The Ets Transcription Factor GABP Is a Component of the Hippo Pathway Essential for Growth and Antioxidant Defense. [链接]

通讯作者：Lanfen Chen　Dawang Zhou（厦门大学）Cell Rep. 2013 May 30;3(5):1663-77. doi: 10.1016/j.celrep.2013.04.020. Epub 2013 May 16.

The transcriptional coactivator Yes-associated protein (YAP) plays an important role in organ-size control and tumorigenesis. However, how Yap gene expression is regulated remains unknown. This study shows that the Ets family member GABP binds to the Yap promoter and activates YAP transcription. The depletion of GABP downregulates YAP, resulting in a G1/S cell-cycle block and increased cell death, both of which are substantially rescued by reconstituting YAP. GABP can be inactivated by oxidative mechanisms, and acetaminophen-induced glutathione depletion inhibits GABP transcriptional activity and depletes YAP. In contrast, activating YAP by deleting Mst1/Mst2 strongly protects against acetaminophen-induced liver injury. Similar to its effects on YAP, Hippo signaling inhibits GABP transcriptional activity through several mechanisms. In human liver cancers, enhanced YAP expression is correlated with increased nuclear expression of GABP. Therefore, we conclude that GABP is an activator of Yap gene expression and a potential therapeutic target for cancers driven by YAP.

RhoGAPs Attenuate Cell Proliferation by Direct Interaction with p53 Tetramerization Domain.[链接]

通讯作者：房静远（上海交通大学医学院）Cell Rep. 2013 May 30;3(5):1526-38. doi: 10.1016/j.celrep.2013.04.017.

Many Rho GTPase activation proteins (RhoGAPs) are deleted or downregulated in cancers, but the functional consequences are still unclear. Here, we show that the RhoGAP ArhGAP11A induces cell-cycle arrest and apoptosis by binding to the tumor suppressor p53. The RhoGAP domain of ArhGAP11A binds to the tetramerization domain of p53, but not to its family members p63 or p73. The interaction stabilizes the tetrameric conformation of p53 and enhances its DNA-binding activity, thereby inducing cell-cycle arrest and apoptosis. Upon DNA damage stress, ArhGAP11A accumulates in the nucleus and interacts with p53, whereas knockdown of ArhGAP11A partially blocks p53 transcriptional activity. These findings explain why RhoGAPs are frequently deleted in cancers and suggest that the RhoGAP family sits at the crossroads between the cell-migration and proliferation pathways.

An Autoinhibited Conformation of LGN Reveals a Distinct Interaction Mode between GoLoco Motifs and TPR Motifs.[链接]

通讯作者：王文宁 张明杰（复旦大学&香港科技大学）Structure. 2013 Jun 4;21(6):1007-17. doi: 10.1016/j.str.2013.04.005. Epub 2013 May 9.

LGN plays essential roles in asymmetric cell divisions via its N-terminal TPR-motif-mediated binding to mInsc and NuMA. This scaffolding activity requires the release of the autoinhibited conformation of LGN by binding of Gαi to its C-terminal GoLoco (GL) motifs. The interaction between the GL and TPR motifs of LGN represents a distinct GL/target binding mode with an unknown mechanism. Here, we show that two consecutive GL motifs of LGN form a minimal TPR-motif-binding unit. GL12 and GL34 bind to TPR0-3 and TPR4-7, respectively. The crystal structure of a truncated LGN reveals that GL34 forms a pair of parallel α helices and binds to the concave surface of TPR4-7, thereby preventing LGN from binding to other targets. Importantly, the GLs bind to TPR motifs with a mode distinct from that observed in the GL/Gαi·GDP complexes. Our results also indicate that multiple and orphan GL motif proteins likely respond to G proteins with distinct mechanisms.

Structural Basis for the Unique Heterodimeric Assembly between Cerebral Cavernous Malformation 3 and Germinal Center Kinase III. [链接]

通讯作者：王大成 丁璟珒（中国科学院生物物理研究所）Structure. 2013 Jun 4;21(6):1059-66. doi: 10.1016/j.str.2013.04.007. Epub 2013 May 9.

Defects in cerebral cavernous malformation protein CCM3 result in cerebral cavernous malformation (CCM), a common vascular lesion of the human CNS. CCM3 functions as an

adaptor protein that interacts with various signal proteins. Among these partner proteins, germinal center kinase III (GCKIII) proteins have attracted significant interest because GCKIII-CCM3 interactions play essential roles in vascular physiology. Here, we report the crystal structures of CCM3 in complex with the C-terminal regulatory domains of GCKIII (GCKIIIct) at 2.4 Å resolution. Our results reveal that GCKIIIct adopts a fold closely resembling that of the CCM3 N-terminal dimeric domain. GCKIIIct heterodimerizes with CCM3 in a manner analogous to CCM3 homodimerization. The remarkable structural rearrangement of CCM3 induced by GCKIIIct binding and the ensuing interactions within CCM3 are characterized as the structural determinants for GCKIIIct-CCM3 heterodimerization. Taken together, these findings provide a precise structural basis for GCKIIIct-CCM3 heterodimerization and the functional performance of GCKIII mediated by CCM3.

SR Proteins Collaborate with 7SK and Promoter-Associated Nascent RNA to Release Paused Polymerase. [链接]

通讯作者：傅向东（武汉大学）Cell. 2013 May 9;153(4):855-68. doi: 10.1016/j.cell.2013.04.028.

RNAP II is frequently paused near gene promoters in mammals, and its transition to productive elongation requires active recruitment of P-TEFb, a cyclin-dependent kinase for RNAP II and other key transcription elongation factors. A fraction of P-TEFb is sequestered in an inhibitory complex containing the 7SK noncoding RNA, but it has been unclear how P-TEFb is switched from the 7SK complex to RNAP II during transcription activation. We report that SRSF2 (also known as SC35, an SR-splicing factor) is part of the 7SK complex assembled at gene promoters and plays a direct role in transcription pause release. We demonstrate RNA-dependent, coordinated release of SRSF2 and P-TEFb from the 7SK complex and transcription activation via SRSF2 binding to promoter-associated nascent RNA. These findings reveal an unanticipated SR protein function, a role for promoter-proximal nascent RNA in gene activation, and an analogous mechanism to HIV Tat/TAR for activating cellular genes.

Sperm, but not oocyte, DNA methylome is inherited by zebrafish early embryos. [链接]

通讯作者：慈维敏 刘江（中国科学院北京基因组研究所&中国科学院大学）Cell. 2013 May 9;153(4):773-84. doi: 10.1016/j.cell.2013.04.041.

5-methylcytosine is a major epigenetic modification that is sometimes called "the fifth nucleotide." However, our knowledge of how offspring inherit the DNA methylome from parents is limited. We generated nine single-base resolution DNA methylomes, including zebrafish gametes and early embryos. The oocyte methylome is significantly hypomethylated compared to sperm. Strikingly, the paternal DNA methylation pattern is maintained throughout early embryogenesis. The maternal DNA methylation pattern is maintained until the 16-cell stage. Then, the oocyte methylome is gradually discarded through cell division and is progressively reprogrammed to a pattern similar to that of the sperm methylome. The passive demethylation rate and the de novo methylation rate are similar in the maternal DNA. By the midblastula stage, the embryo's methylome is virtually identical to the sperm methylome. Moreover, inheritance of the

sperm methylome facilitates the epigenetic regulation of embryogenesis. Therefore, besides DNA sequences, sperm DNA methylome is also inherited in zebrafish early embryos.

Adiponectin Mediates the Metabolic Effects of FGF21 on Glucose Homeostasis and Insulin Sensitivity in Mice. [链接]

通讯作者：李校堃 徐爱民（温州医学院&香港大学）Cell Metab. 2013 May 7;17(5):779-89. doi: 10.1016/j.cmet.2013.04.005.

Fibroblast growth factor 21 (FGF21) is a metabolic hormone with pleiotropic effects on regulating glucose and lipid homeostasis and insulin sensitivity. However, the mechanisms underlying the metabolic actions of FGF21 remain unknown. Here we show that the insulin-sensitizing adipokine adiponectin is a downstream effector of FGF21. Treatments with FGF21 enhanced both expression and secretion of adiponectin in adipocytes, thereby increasing serum levels of adiponectin in mice. Adiponectin knockout mice were refractory to several therapeutic benefits of FGF21, including alleviation of obesity-associated hyperglycemia, hypertriglyceridemia, insulin resistance, and hepatic steatosis. Furthermore, the effects of FGF21 on attenuation of obesity-induced impairment in insulin signaling in liver and skeletal muscle were abrogated in adiponectin knockout mice, whereas FGF21-mediated activation of ERK1/ERK2 in adipose tissues remained unaffected. Therefore, adiponectin couples FGF21 actions in local adipocytes to liver and skeletal muscle, thereby mediating the systemic effects of FGF21 on energy metabolism and insulin sensitivity.

3、Science 及其子刊

Molecular basis of age-dependent vernalization in Cardamine flexuosa.[链接]

通讯作者：王佳伟（中国科学院上海生命科学研究院）Science. 2013 May 31;340 (6136):1097-100.

Plants flower in response to many varied cues, such as temperature, photoperiod, and age. The floral transition of Cardamine flexuosa, a herbaceous biennial-to-perennial plant, requires exposure to cold temperature, a treatment known as vernalization. C. flexuosa younger than 5 weeks old are not fully responsive to cold treatment. We demonstrate that the levels of two age-regulated microRNAs, miR156 and miR172, regulate the timing of sensitivity in response to vernalization. Age and vernalization pathways coordinately regulate flowering through modulating the expression of CfSOC1, a flower-promoting MADS-box gene. The related annual Arabidopsis thaliana, which has both vernalization and age pathways, does not possess an age-dependent vernalization response. Thus, the recruitment of age cue in response to environmental signals contributes to the evolution of life cycle in plants.

Infectivity, Transmission, and Pathology of Human H7N9 Influenza in Ferrets and Pigs. [链接]

通讯作者：管轶（汕头大学医学院）Science. 2013 May 23. [Epub ahead of print]

The emergence of the H7N9 influenza virus in humans in Eastern China has raised concerns that a new influenza pandemic could occur. Here, we used a ferret model to evaluate the infectivity and transmissibility of A/Shanghai/2/2013 (SH2), a human H7N9 virus isolate. This virus replicated in the upper and lower respiratory tracts of the ferrets and was shed at high titers for 6 to 7 days, with ferrets showing relatively mild clinical signs. SH2 was efficiently transmitted via direct contact, but less efficiently by airborne exposure. Pigs could be productively infected by SH2 and shed virus for 6 days but were unable to transmit the virus to other animals. Under appropriate conditions human-to-human transmission of the H7N9 virus may be possible.

An Increase in Synaptic NMDA Receptors in the Insular Cortex Contributes to Neuropathic Pain.[链接]

通讯作者：招明高 卓敏（中国人民解放军第四军医大学&西安交通大学）Sci Signal. 2013 May 14;6(275):ra34. doi: 10.1126/scisignal.2003778.

Neurons in the insular cortex are activated by acute and chronic pain, and inhibition of neuronal activity in the insular cortex has analgesic effects. We found that in a mouse model in which peripheral nerve injury leads to the development of neuropathic pain, the insular cortex showed changes in synaptic plasticity, which were associated with a long-term increase in the amount of synaptic N-methyl-d-aspartate receptors (NMDARs), but not that of extrasynaptic NMDARs. Activation of cyclic adenosine monophosphate (cAMP)-dependent signaling enhanced the amount of synaptic NMDARs in acutely isolated insular cortical slices and increased the surface localization of NMDARs in cultured cortical neurons. We found that the increase in the amount of NMDARs required phosphorylation of the NMDAR subunit GluN2B at Tyr(1472) by a pathway involving adenylyl cyclase subtype 1 (AC1), protein kinase A (PKA), and Src family kinases. Finally, injecting NMDAR or GluN2B-specific antagonists into the insular cortex reduced behavioral responses to normally nonnoxious stimuli in the mouse model of neuropathic pain. Our results suggest that activity-dependent plasticity takes place in the insular cortex after nerve injury and that inhibiting the increase in NMDAR function may help to prevent or treat neuropathic pain.

H5N1 Hybrid Viruses Bearing 2009/H1N1 Virus Genes Transmit in Guinea Pigs by Respiratory Droplet.[链接]

通讯作者：陈化兰（中国农业科学院）Science. 2013 May 2.

In the past, avian influenza viruses have crossed species' barriers to trigger human pandemics by reassorting with mammal-infective viruses in intermediate livestock hosts. H5N1 viruses are able to infect pigs, and some of them have affinity for the mammalian type α-2,6-linked sialic acid airway receptor. By using reverse genetics, we systemically created 127 reassortant viruses between a duck isolate of H5N1, specifically retaining its hemagglutinin (HA) gene throughout, and a highly transmissible, human-infective H1N1 virus. We tested the virulence of the reassortants in mice as a correlate for virulence in humans, and tested transmissibility in guinea

pigs, which have both avian and mammalian types of airway receptor. Transmission study showed that both polymerase PA gene and nonstructural protein NS gene of H1N1 virus made the H5N1 virus transmissible by respiratory droplet between guinea pigs, without death. Further experiments implicated other H1N1 genes in the enhancement of mammal-to-mammal transmission, including nucleoprotein (NP), neuraminidase (NA), and matrix (M), as well as mutations in H5 HA that improve affinity for human-like airway receptors. Hence, avian H5N1 subtype viruses do have the potential to acquire mammalian transmissibility by reassortment in current agricultural scenarios.

An Airborne Transmissible Avian Influenza H5 Hemagglutinin Seen at the Atomic Level.[链接]

通讯作者：高福（中国科学院微生物研究所）Science. 2013 May 2.

Recent studies have identified several mutations in the hemagglutinin (HA) protein that allow the highly pathogenic avian H5N1 influenza A virus to transmit between mammals by airborne route. Here, we determined the complex structures of wild-type and mutant HAs derived from an Indonesia H5N1 virus bound to either avian or human receptor sialic acid analogs. A cis/trans conformational change in the glycosidic linkage of the receptor analog was observed, which explains how the H5N1 virus alters its receptor binding preference. Furthermore, the mutant HA possessed low affinities for both avian and human receptors. Our findings provide a structural and biophysical basis for the H5N1 adaptation to acquire human, but maintain avian, receptor binding properties.