科学需要人们全部生命去探索

王应睐

中国科学院生物化学与细胞生物学研究所
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中科院生化与细胞所

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# 中科院生化与细胞所

中国科学院
生物化学与细胞生物学研究所

2012

# 中科院生化与细胞所

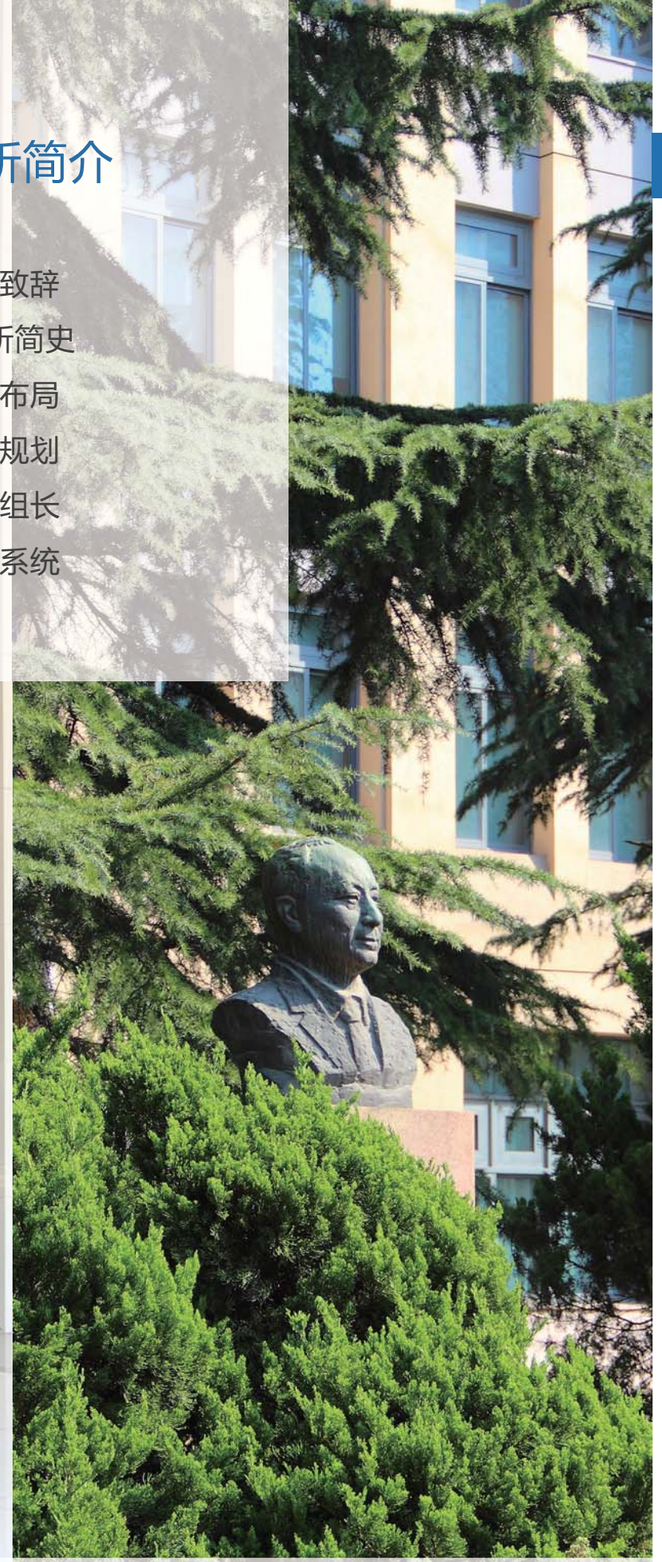


欢迎来到中国科学院生物化学与细胞生物学研究所。

生化与细胞所岳阳路园区

# 研究所简介



位于生化楼一楼门厅内的原生化所首任所长王应睐铜像(左)和
位于细胞楼正门前的原实生所第二任所长朱洗铜像(右)

## 所长致辞

林安宁 博士
研究员，所长

中国科学院生物化学与细胞生物学研究所成立于 2000 年 5 月，由原中国科学院上海生物化学研究所 (1950-2000 年 ) 与原中国科学院上海细胞生物学研究所 (1950-2000 年 ) 整合而成。在王应睐、朱洗等前辈科学家的带领下，并经过几代科学家的共同努力，生化与细胞所与其前身研究所的科研人员在过去半个多世纪的创业和奋斗中，取得了人工全合成结晶牛胰岛素、人工合成酵母丙氨酸转移核糖核酸、卵母细胞的受精成熟和单性生殖等国际领先重大成果，多次获得国家自然科学一等奖、国家科技进步一等奖。

生化与细胞所致力于生命科学基础研究，研究内容涵盖生物化学、分子生物学、细胞生物学等学科领域，在分子生物学国家重点实验室、细胞生物学国家重点实验室、国家蛋白质科学综合研究中心 ( 上海 ) 等三大研究集群的有力支撑下，着重开展“基因调控、RNA 与表观遗传学”、“蛋白质科学”、“细胞信号转导”、“细胞与干细胞生物学”、“癌症和其它重大疾病”等五大领域的研究。

生化与细胞所的使命是开展创造性的生命科学研究 ,并为促进国民健康服务。生化与细胞所的目标是成为国际一流研究所，努力为科学家提供自由探索和团队合作的学者型研究环境，为研究生、博士后和其他研究人员提供高标准的、系统性的训练。

生命科学无疑是 21 世纪最重要的学科之一。生物化学、分子生物学、细胞生物学的研究，将致力于破译生命的奥秘，并为现代医学提供生物学理论基础和医疗靶点。我相信生化与细胞所将继续为此做出中国科学家应有的贡献。

# 研究所简史

中国科学院上海生物化学研究所（生化所）前身是1950年成立的中国科学院生理生化研究所的生化大组。从1950年到2000年，生化所发表科学论文近 4000 篇，取得国家、部委、省、市级获奖科研成果 178 项（其中国家一等奖 4 项、二等奖 9 项），培养研究生 255 人，博士生 171 人。

中国科学院上海细胞生物学研究所（细胞所）前身是1950年成立的中国科学院实验生物研究所（实生所）。从1950年到2000年，细胞所发表科学论文近 1600 篇，取得国家、部委、省、市级获奖科研成果 92 项（其中国家一等奖 1 项、二等奖 2 项），培养研究生 112 人，博士生 107 人。

2000 年，生化所与细胞所整合成立中国科学院生物化学与细胞生物学研究所（生化与细胞所）。


**1958** 岳阳路园区大门，左侧竖匾上有“中国科学院实验生物研究所”，右侧竖匾上有“中国科学院生物化学研究所”（1958 年左右）



研究所简史

## 生化所

**1959**


国庆十周年生化所全体职工合影
（9 月 30 日）

钮经义（中）等讨论多肽合成新途径

**1986**

国家计委和中科院召开分子生物学国家重点实验室验收会
（12 月 17 日）

**1997**


庆祝生化所建所四十周年大会暨贺王应睐先生九十寿辰
（11 月 13 日）

**1999**

生化所实验大楼

## 细胞所

**1961**

朱洗（左二）分析讲解蟾蜍人工单性生殖研究实验记录

**1981**


“文革”后首次恢复招收的 1978 级研究生毕业与导师合影

**1985**

马普客座实验室成立剪彩仪式
（4 月 4 日）

**1991**

庄孝德、王亚辉、郭礼和陪同德方代表视察马普客座实验室

**1999**

细胞所实验大楼

# 研究所简史

## 人工全合成结晶牛胰岛素

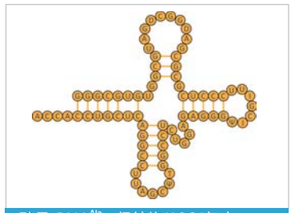
牛胰岛素一级结构(1951年由Frederick Sanger测定序列)

科研人员在进行人工合成牛胰岛素活力测定

1978年12月14日，聂荣臻副总理在北京人民大会堂接见参加胰岛素总评会的全体同志

1982年获国家自然科学一等奖

- 1958 提出人工全合成牛胰岛素项目
- 1959 天然胰岛素拆合成功
- 1960 人工合成胰岛素开始全国性协作 / 胰岛素 A 链和 B 链合成成功 / 合成胰岛素大兵团作战
- 1963 全国性协作再次启动，包括生化所、北大化学系和有机所
- 1964 人工合成胰岛素 A、B 链第一次组合成功 ( 出现微弱活性 )
- 1965 人工合成结晶牛胰岛素成功，这是世界上第一次用人工方法合成具有与天然分子相同化学结构和完整生物活性的蛋白质
- 1966 《科学》杂志刊登“红色中国的胰岛素全合成”报道中国人工合成胰岛素成果
- 1982 人工合成牛胰岛素获得国家自然科学一等奖



酵母tRNA$^{Ala}$一级结构(1964年由Robert W. Holley测定序列)

王德宝(中)与协作组部分成员

## 人工全合成酵母丙氨酸转移核糖核酸 (tRNA$^{Ala}$)

- 1967 提出人工合成酵母 tRNA$^{Ala}$ 项目
- 1968 人工合成酵母 tRNA$^{Ala}$ 项目启动，上海方面由生化所负责，细胞所、有机所参加
- 1974 成功合成一个八核苷七磷酸片段
- 1977 中科院成立人工合成酵母 tRNA$^{Ala}$ 协作组
- 1978 成立三个会战组 ( 大片段、总装、测活 )
- 1981 人工合成酵母 tRNA$^{Ala}$ 成功，这是世界上第一次用人工方法合成具有与天然分子相同化学结构和完整生物活性的核糖核酸
- 1983 《自然》杂志刊登“核酸合成，拼音 tRNA”报道中国人工合成 tRNA$^{Ala}$ 成果
- 1987 人工合成酵母 tRNA$^{Ala}$ 获得国家自然科学一等奖

1982年1月18日参加中科院在北京科学会堂召开的人工合成酵母tRNA$^{Ala}$ 学术报告会的人员合影

1987年获国家自然科学一等奖



# 学科布局

## 三大研究集群

( 详情请见 55 - 60 页 )

### 分子生物学 国家重点实验室

李　林
主任

### 细胞生物学 国家重点实验室

朱学良
主任

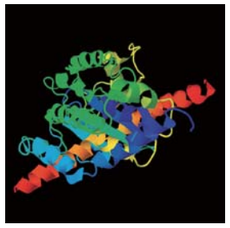
### 国家蛋白质科学 综合研究中心(上海)

雷　鸣
主任

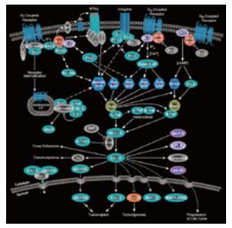
## 五大研究领域

(详情请见15 - 50页)

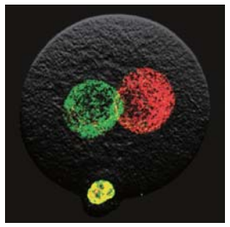
基因调控、RNA、表观遗传学



蛋白质科学



细胞信号转导



细胞与干细胞生物学

癌症和其它重大疾病

# 战略规划

## 发展理念

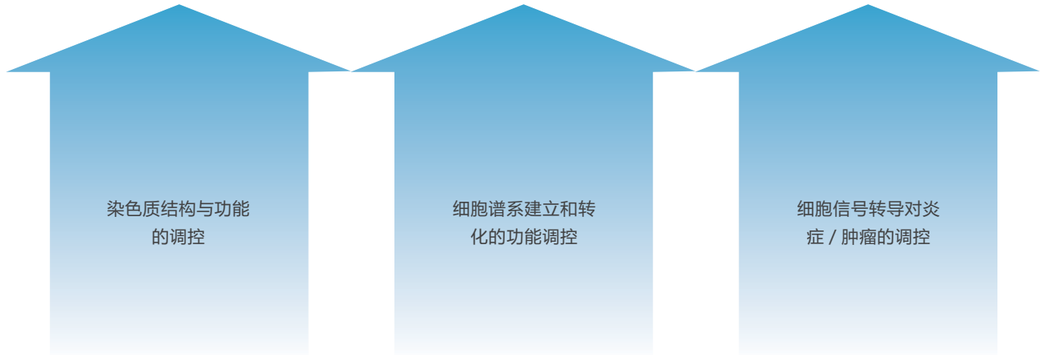
- 营造一个学者型研究环境
- 创建一个国际一流研究所

拥有一批具有国际一流水平教授，他们系统性、持续性地做出开拓性的工作，在一些重大研究方向 / 领域成为国际公认的学术权威。

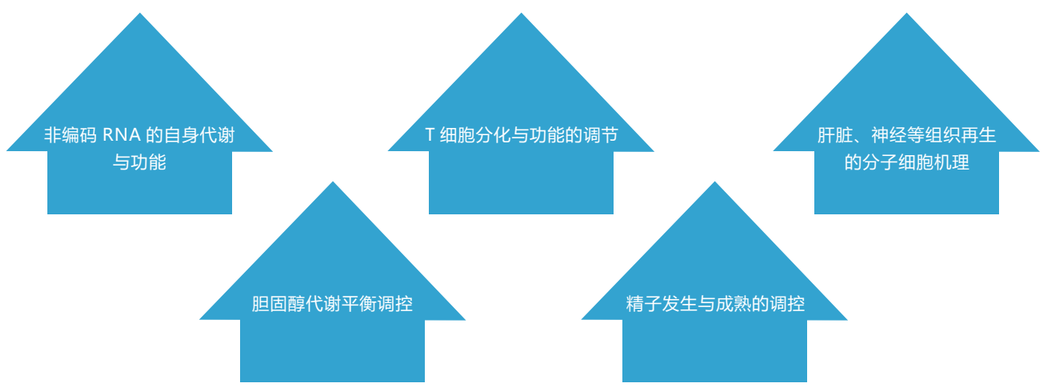
## 使命定位

定位于基础研究，以提升国家自主创新能力和建设国际一流研究所为目标，致力于生物化学与分子生物学、细胞生物学的前沿基础研究，聚集与培养相关学科高端人才，为人口与健康等国家重大需求提供源头创新成果。

## 三个重大突破目标




## 五个重点培育方向

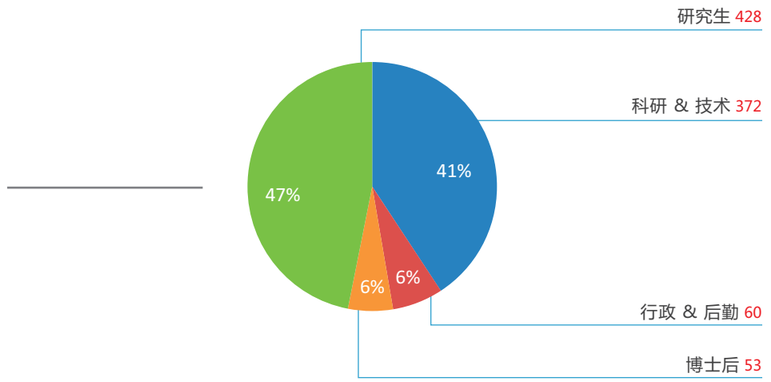


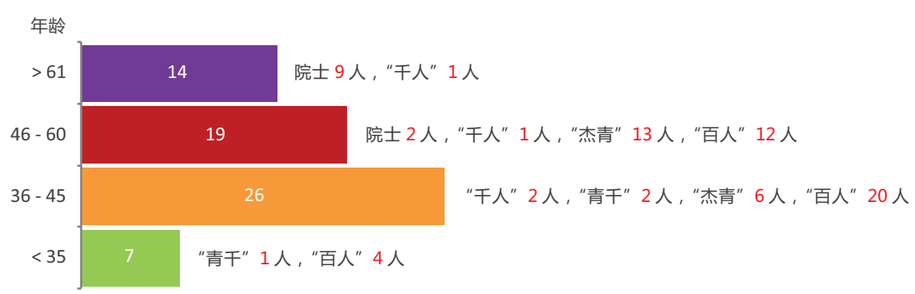



# 研究组长

截至 2012 年 7 月底，研究所总人数 913 人，其中研究组长 (PI) 66 人，包括中国科学院院士 10 人，中国工程院院士 1 人，中组部“千人计划”人才 4 人 ,中组部“青年千人计划” 3 人，国家“杰出青年”科学基金获得者 19 人，中科院“百人计划”人才 36 人。

研究所人员分布 (2012 年 7 月 )



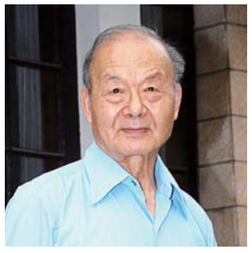

研究组长年龄结构 (2012 年 7 月 )

## 研究组长奖励荣誉(2009-2012)

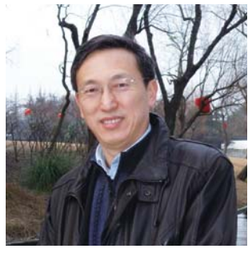
| 研究组长 | 奖励荣誉名称 | 年度 |
|---|---|---|
| 宋保亮 | 陈嘉庚青年科学奖 | 2012 |
| 裴　钢 | 谈家桢生命科学成就奖 | 2011 |
| 惠利健 | 中国青年科技奖 | 2011 |
| 周金秋 | A-IMBN Arthur Kornberg Memorial Award | 2011 |
| 刘小龙 | A-IMBN Research Young Investigators Award | 2011 |
| 裴　钢 | 陈嘉庚科学奖 | 2010 |
| 景乃禾 | 上海市领军人才 | 2010 |
| 刘小龙 | 中国青年科技奖 | 2009 |
| 朱学良 | 上海市自然科学牡丹奖 | 2009 |

刘新垣 研究员 中科院院士，1991年当选
癌症的生物治疗

龚岳亭 研究员 中科院院士，1993年当选
活性肽和蛋白的结构功能



李载平 研究员 工程院院士，1995年当选
HBV/肝癌相关基因检定与功能



洪国藩 研究员 中科院院士，1997年当选
共生固氮体系中Small RNA功能

裴　钢 研究员 中科院院士，1999年当选
细胞信号转导

戚正武 研究员 中科院院士，1999年当选
活性多肽及酶蛋白的结构功能

张友尚 研究员 中科院院士，2001年当选
蛋白质的结构与功能

张永莲 研究员 中科院院士，2001年当选
精子在附睾中成熟的分子基础

林其谁 研究员 中科院院士，2003年当选
生物膜结构与功能

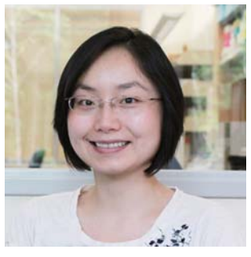
王恩多 研究员 中科院院士，2005年当选
蛋白质生物合成的质量控制

李　林 研究员 中科院院士，2011年当选
细胞信号转导与调控的分子机制与功能

鲍　岚 研究员
神经细胞蛋白质运输

陈德桂 研究员
表观遗传、干细胞和癌症

陈剑峰 研究员
炎症与癌症中细胞粘附分子的功能调控

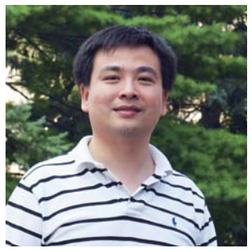


陈江野 研究员
形态发生的基因表达调控

陈玲玲 研究员
长非编码RNA和干细胞

陈正军 研究员
磷酸化蛋白质信号网络与肿瘤发生

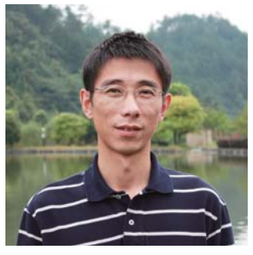




陈　勇 研究员
表观遗传调控的结构生物学

程　红 研究员
基因表达的调控与功能

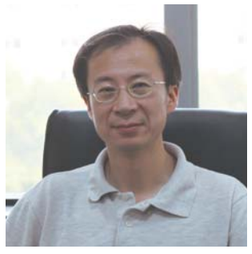
丛　尧 研究员
分子伴侣协助下蛋白质折叠与解聚的结构生物学

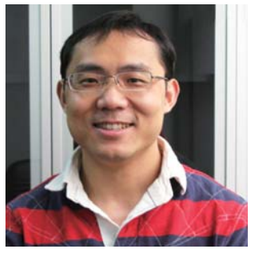


丁建平 研究员
真核基因表达的结构生物学

高大明 研究员
癌症信号转导与代谢

葛高翔 研究员
细胞微环境对肿瘤发生及转移的调控





何勇宁 研究员
细胞表面受体以及细胞间相互作用的结构生物学研究

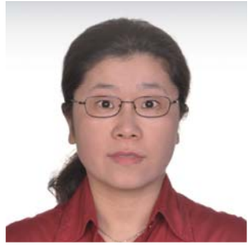
侯法建 研究员
天然免疫中信号转导的生化机理

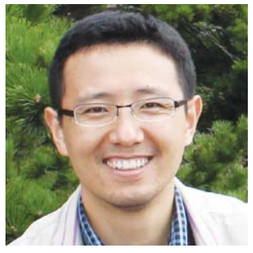
胡红雨 研究员
蛋白质错误折叠和降解作用

胡　苹 研究员
成体干细胞的命运决定

胡荣贵 研究员
蛋白质降解调控与分子识别

黄　昊 研究员
基因转录调控的结构生物学研究

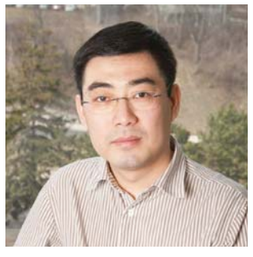




惠静毅 研究员
RNA加工的调控

惠利健 研究员
肝脏疾病的分子病理机制

季红斌 研究员
肺癌发病的分子机理



姜　海 研究员
癌症的个体化治疗和新型抗癌药物的筛选开发

景乃禾 研究员
干细胞与神经发育

雷　鸣 研究员
染色质的结构生物学

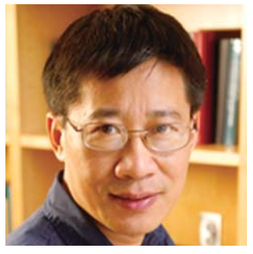
**李伯良 研究员**
胆固醇代谢平衡的基因表达调控

**李劲松 研究员**
体细胞重编程与诱导多能干细胞

**李逸平 研究员**
生殖细胞与胚胎发育

**廖　侃 研究员**
细胞增殖与分化的调控

**廖鲁剑 研究员**
功能蛋白质组学；神经退行性疾病
的信号传导研究



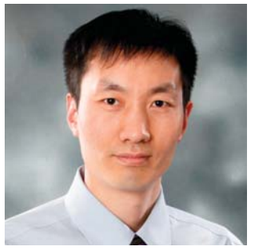
**林安宁 研究员**
信号转导与基因调控

**刘定干 研究员**
抑癌核酸元件的功能及其调控

**刘默芳 研究员**
非编码RNA在癌症发生和精子发生
中的功能机制

**刘小龙 研究员**
免疫细胞分化与功能

**阮康成 研究员**
生物大分子结构功能和相互作用的
光谱学研究



**宋保亮 研究员**
胆固醇代谢关键蛋白及其功能调控

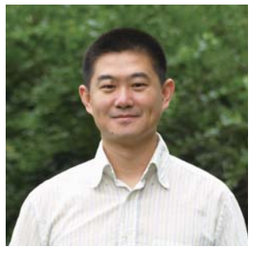
**宋建国 研究员**
细胞分化与凋亡机理及其在癌症
发展中的作用

**王　琛 研究员**
宿主细胞防御调控

**王　纲 研究员**
真核基因表达调控以及
癌症与干细胞生物学

**王红艳 研究员**
淋巴细胞活化和粘附的分子机制

**吴家睿 研究员**
细胞活动的蛋白质调控网络以及
复杂疾病的系统生物学研究



**吴立刚 研究员**
非编码小RNA作用机制

**许琛琦 研究员**
淋巴细胞的信号转导



**徐国良 研究员**
表观遗传调控及其与癌症等
重大疾病的关系

**曾　嵘 研究员**
蛋白质组学与蛋白质动态行为

**曾　艺 研究员**
成体干细胞的信号调控及
干细胞与微环境的相互作用

**张　雷 研究员**
发育过程的组织分化与生长调控

**张学军 研究员**
细胞凋亡的分子机制及其在疾病
中的作用

**赵慕钧 研究员**
肿瘤相关基因的功能及其调控

**赵　允 研究员**
细胞内信号传导通路的异常与
疾病发生的分子基础

**周界文 研究员**
跨膜转运的分子机制

**周金秋 研究员**
染色质与细胞衰老

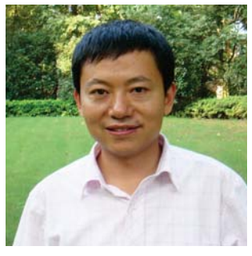
**周兆才 研究员**
GCK激酶信号转导的结构与
分子机制

**朱学良 研究员**
细胞周期与运动

**邹卫国 研究员**
骨的发育与衰老的分子基础

## 兼职研究员

**张荣光 研究员**
蛋白质结构与功能，结构生物学
技术与方法



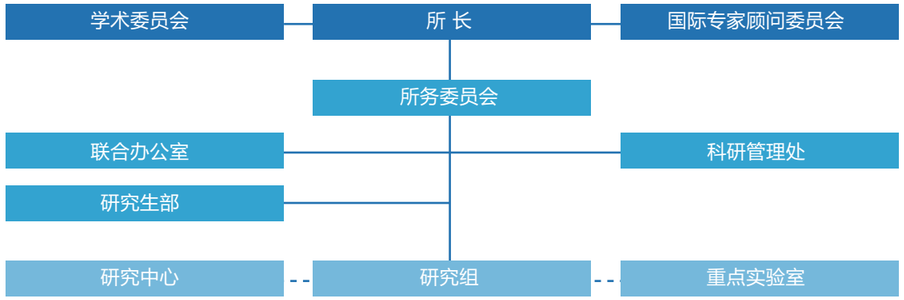
## 客座研究员

**李党生 研究员**
Cell Research常务副主编

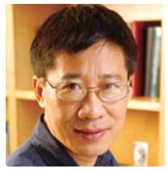
**孙　兵 研究员**
树突状细胞的成熟以及辅助性
T细胞的分化调控

# 行政系统

## 行政组织架构




## 研究所领导



林安宁
所长

景乃禾
党委书记、常务副所长

朱学良
副所长

周金秋
副所长

雷　鸣
副所长

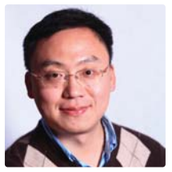
郭金华
党委副书记

陈正军
所长助理

王　纲
所长助理

江　舸
所长助理

## 行政部门负责人



江　舸
科研管理处处长

宋金芳
联合办公室主任

薄祥慧
研究生部副主任 (主持工作)



行政楼前的月桂树

# 研究与转化



**小分子RNA调控纤毛发生**

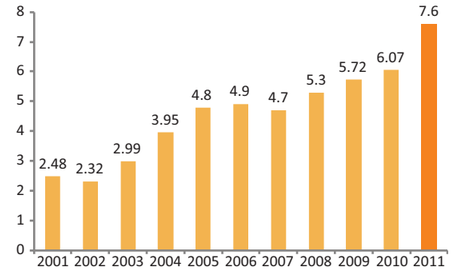
在培养的HEK293T细胞中，过量表达小分子RNA miR-129-3p诱导增殖中的细胞长出纤毛。

# 科研概况

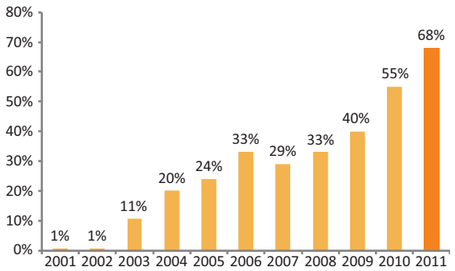
## 论文发表

2009 - 2012 年 7 月，研究所共发表 SCI 论文 388 篇，其中：

- 在国际顶尖期刊发表论文 6 篇，包括 Cell 2 篇，Nature 3 篇，Science 1 篇。
- 在国际一流期刊发表论文 59 篇，包括 Cell Stem Cell 2 篇，Developmental Cell 3 篇，Molecular Cell 1 篇，Cell Metabolism 2 篇，Nature Immunology 2 篇，Nature Cell Biology 2 篇，Nature Structural & Molecular Biology 1 篇，Neuron 1 篇，Proceedings of the National Academy of Sciences USA 10 篇，EMBO Journal 3 篇，PLoS Biology1 篇，PLoS Genetics 2 篇，Gastroenterology 2 篇，Hepatology 4 篇以及 Blood 2 篇。




2001-2011 年研究所发表 SCI 论文篇均 IF

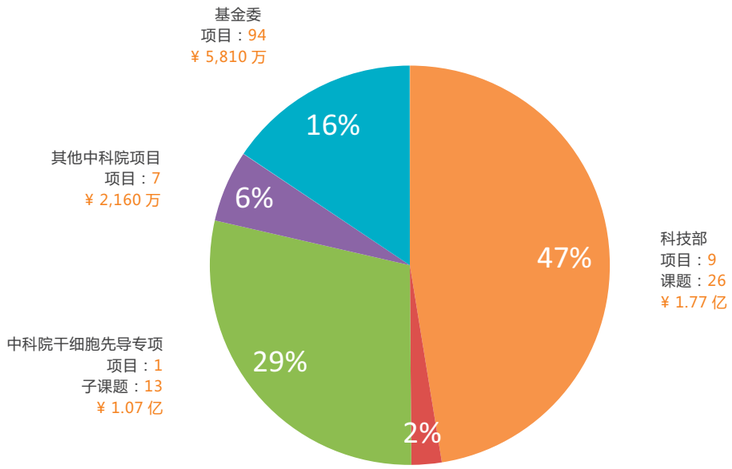



2001-2011 年研究所发表 IF ≥JBC 论文占全部 SCI 论文比例

## 科研奖励和荣誉(2001-2011)

| 时间 | 成果 | 奖励/荣誉 |
|---|---|---|
| 2011 | 将小鼠成纤维细胞成功转化为功能性肝细胞样细胞 | 中国科学十大进展 |
| | 揭示Tet双加氧酶在哺乳动物表观遗传调控中的重要作用 | |
| 2009 | 发现β-抑制因子-2复合体信号缺损可导致胰岛素耐受 | 中国基础研究十大新闻 |
| 2007 | 发现β抑制因子-1是调节$CD4^+$T细胞存活和自身免疫性的关键因子 | |
| 2008 | 精子在附睾中成熟的分子基础研究 | 国家自然科学奖二等奖 |
| 2007 | G蛋白偶联受体信号与其它细胞信号通路间的对话机制 | |
| 2005 | 核糖体失活蛋白与核糖体RNA结构与功能的研究 | |
| 2001 | 氨基酰-tRNA合成酶及其与相关tRNA的相互作用 | |
| 2002 | 重组人表皮生长因子 | 国家科技进步奖二等奖 |

2009 - 2011 年，研究所新增科技部、基金委、中科院及上海市科委竞争性科研项目（ 课题 ）共 184 项，获得竞争性经费 3.73 亿元。




## 重大科研项目(2009-2011)

| 年份 | 名称 | 类别 | 负责人 |
|---|---|---|---|
| 2011 | 细胞谱系的建立与发育调控 | 中科院“干细胞与再生医学研究”战略性先导科技专项 | 景乃禾 |
| 2009 | 炎症过程中细胞间相互作用的信号转导机制及其应用研究 | 科技部973计划项目 | 陈剑峰 |
| 2011 | 炎症诱导肿瘤的分子调控网络研究 | 科技部重大科学研究计划项目 | 林安宁 |
| 2011 | 上皮组织的形成、更新及其调节机理 | | 朱学良 |
| 2010 | 亚细胞代谢调控及其相关老年痴呆症等疾病机理 | | 李伯良 |
| 2010 | 基于上海同步辐射光源的结构生物学技术和方法研究 | | 张荣光 |
| 2010 | 干细胞编程与重编程中表观遗传调控的分子机制和结构基础 | | 丁建平 |
| 2009 | 细胞生长调控的重要蛋白质群的功能与作用机制 | | 李　林 |



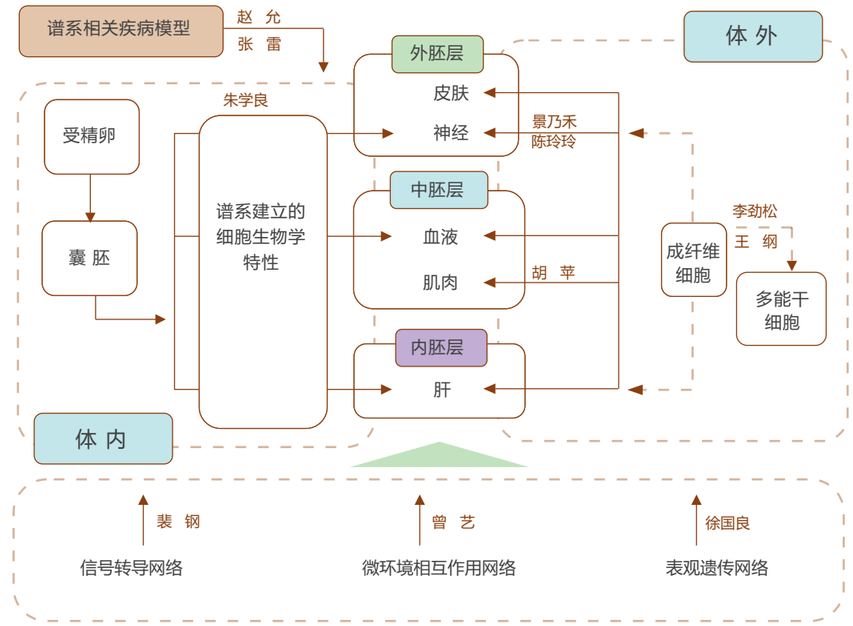


## 干细胞战略性先导科技专项

“干细胞与再生医学研究”战略性先导科技专项是中科院第一批启动的战略先导专项中唯一的生物口专项，是“创新 2020”实施方案的重要组成部分，第一期执行期 5 年 (2011-2015)，总合同经费约 9.2 亿元。

生化与细胞所积极承担专项科研任务，景乃禾研究员担任专项项目一“细胞谱系的建立与发育调控”负责人，13 位研究员担任专项项目一、二、四学术骨干，获得子课题合同经费共计 1.07 亿元。自 2011 年初专项启动以来，研究所参与专项的研究团队在干细胞研究方面取得重大进展，至 2012 年 7 月底已发表 Cell 1 篇，Nature 2 篇，Science 1 篇，Cell Stem Cell 1 篇，Developmental Cell 1 篇，Molecular Cell 1 篇，Nature Cell Biology 1 篇。

项目一： 细胞谱系的建立与发育调控




项目一：研究布局

项目二： 功能性细胞获得的关键技术

课题三　惠利健

项目四： 干细胞应用策略的集成研究

课题四　陈德桂

# 技术平台

截至 2012 年 5 月底，所级公共技术服务中心有技术支撑人员 61 人，其中高级 5 人、中级 21 人、初级 35 人，管理着 7 个技术支撑平台，总价值超过 9000 万元的公共仪器设备。

## 分子生物学技术平台

核酸分析
生物大分子相互作用分析
分子成像
光谱分析
色谱分析
核磁分析
质谱分析

## 细胞分析技术平台

激光扫描共聚焦显微成像
荧光显微成像
活细胞成像
流式细胞术
电子显微镜

## 化学生物学技术平台

高通量小分子化合物筛选
全基因组 RNA 干扰筛选

## 干细胞技术平台

胚胎干细胞建系
小鼠及细胞基因修饰
检测服务
组织学分析





## 动物实验技术平台

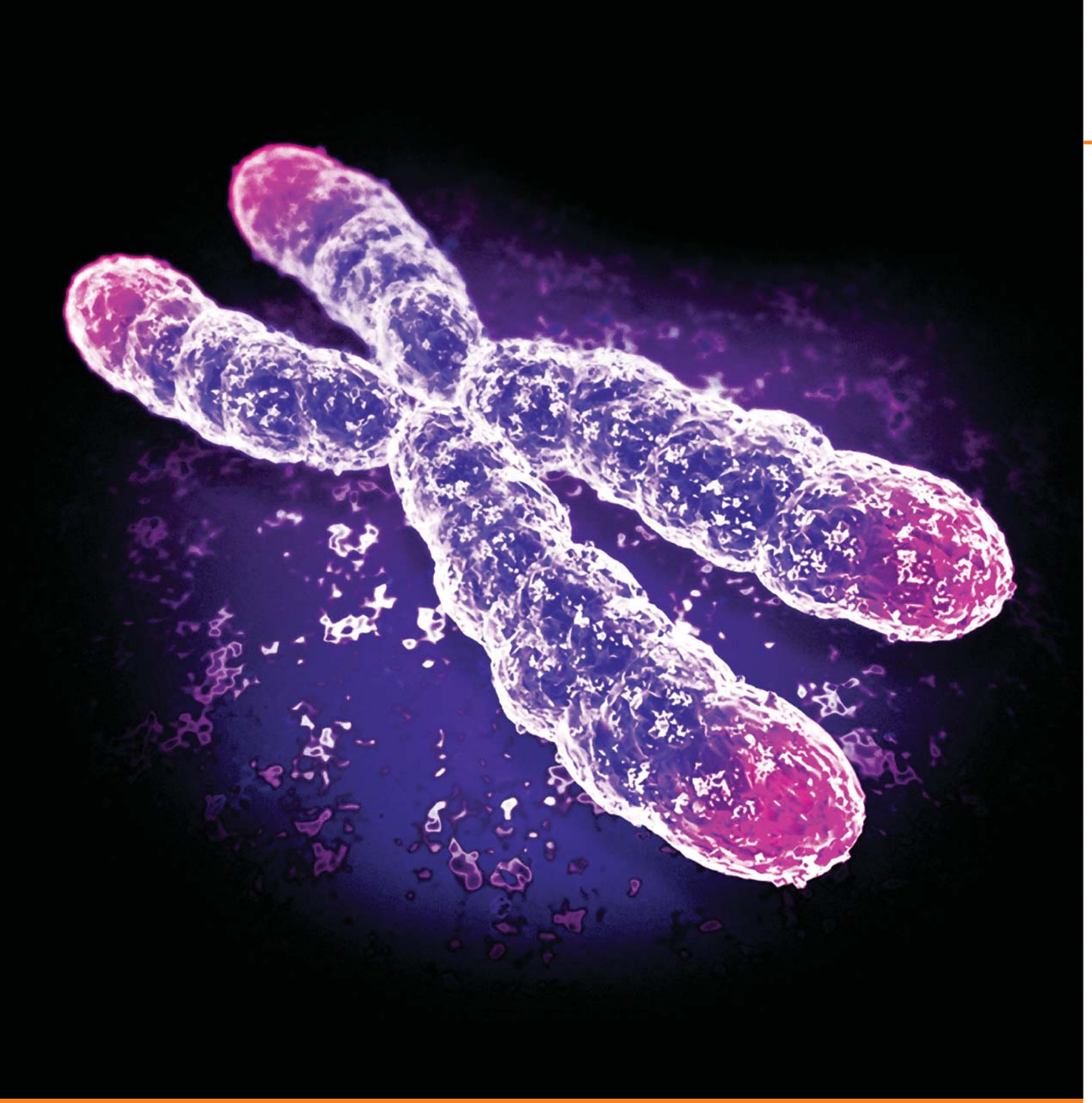
动物饲养
影像学分析
行为学分析
胚胎操作
转基因制作

## 果蝇技术平台

品系引进及饲养
突变体交流及制备
基因克隆
显微注射

## 斑马鱼技术平台

品系引进及饲养
转基因及基因敲除
体视荧光显微成像
胚胎显微注射



## 科研亮点

### 基因调控、RNA、表观遗传学

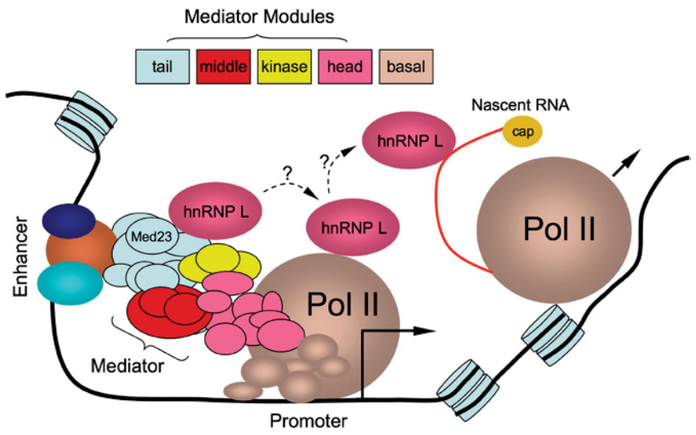
基因调控
RNA生物学
DNA甲基化
组蛋白修饰
端粒生物学



## 中介体复合物偶联转录和剪接
## The Mediator complex couples transcription and splicing

Mediator complex is an integrative hub for transcriptional regulation. Researchers led by Prof. Gang Wang show that Mediator regulates alternative mRNA processing via its MED23 subunit. Combining tandem affinity purification and mass spectrometry, they identified a number of mRNA processing factors that bind to a soluble recombinant Mediator subunit, MED23, but not to several other Mediator components. One of these factors, hnRNP L, specifically interacts with MED23 *in vitro* and *in vivo*. Consistently, Mediator partially colocalizes with hnRNP L and the splicing machinery in the cell. Functionally, MED23 regulates a subset of hnRNP L-targeted alternative splicing (AS) and alternative cleavage and polyadenylation (APA) events, as shown by minigene reporters and exon array analysis. ChIP-seq analysis revealed that MED23 can regulate hnRNP L occupancy at their coregulated genes. Taken together, these results demonstrate a crosstalk between Mediator and the splicing machinery, providing a molecular basis for coupling mRNA processing to transcription.

参考文献: Huang et al. (2012) *Mol. Cell* 45:459-69




Initiating the coupling between transcription and RNA processing at gene promoter. hnRNP L is initially recruited to gene promoter via direct protein-protein interaction with Med23, a tail component of the large Mediator complex. This recruitment appears to also enhance Pol II binding at gene promoter. The recruited hnRNP L affects downstream splicing events by binding to CA-rich motifs in pre-mRNA, although the mechanism for the RNA binding protein to switch from Mediator to elongating Pol II and then to nascent RNA remains to be defined. This work highlights a new role of Mediator in coupling between transcription and pre-mRNA processing. Specific RNA binding proteins recruited to Mediator may also play critical roles in promoting enhancer-promoter communications via intergenic noncoding RNAs. [From Ji X, Fu XD (2012) *Mol. Cell* 45:433-4]

### 重点参考文献

Yin JW, Liang Y, Park JY, Chen D, Yao X, Xiao Q, Liu Z, Jiang B, Fu Y, Bao M, Huang Y, Liu Y, Yan J, Zhu MS, Yang Z, Gao P, Tian B, Li D, Wang G (2012) Mediator MED23 plays opposing roles in directing smooth muscle cell and adipocyte differentiation. *Genes Dev.* [Epub ahead of print]

Wang W*, Huang L*, Huang Y, Yin JW, Berk AJ, Friedman JM, Wang G (2009) Mediator MED23 links insulin signaling to the adipogenesis transcription cascade. *Dev. Cell* 16:764-771

Huang G*, Wang H*, Chou S, Nie X, Chen J#, Liu H# (2006) Bistable expression of WOR1, a master regulator of white-opaque switching in *Candida albicans*. *Proc. Natl. Acad. Sci. U S A* 103:12813-18

### 延伸参考文献

Lei L, Xiong Y, Chen J, Yang JB, Wang Y, Yang XY, Chang CC, Song BL, Chang TY, Li BL (2009) TNF-alpha stimulates the ACAT1 expression in differentiating monocytes to promote the CE-laden cell formation. *J. Lipid Res.* 50:1057-67.

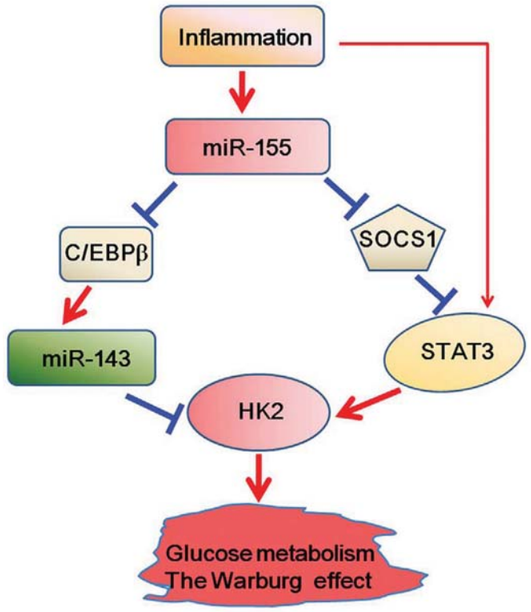
Lu Y, Su C, Mao X, Raniga PP, Liu H#, Chen J# (2008) Efg1-mediated recruitment of NuA4 to promoters is required for hypha-specific Swi/Snf binding and activation in *Candida albicans*. *Mol. Biol. Cell* 19:4260-72

Chen XC*, Feng J*, Hou BH, Li FQ, Li Q, Hong GF (2005) Modulating DNA bending affects NodD-mediated transcriptional control in *Rhizobium leguminosarum*. *Nucleic Acids Res.* 33:2540-8

## 小分子RNA miR-155关联炎症与Warburg效应
## MicroRNA-155 links inflammation to the Warburg effect

Cancer cells preferentially metabolize glucose through aerobic glycolysis. This phenomenon, known as the Warburg effect, is an anomalous characteristic of glucose metabolism in cancer cells. Chronic inflammation is a key promoting factor of tumourigenesis. It remains, however, largely unexplored whether and how pro-tumourigenic inflammation regulates glucose metabolism in cancer cells. Researchers led by Prof. Mofang Liu show that pro-inflammatory cytokines promote glycolysis in breast cancer cells, and that the inflammation-induced miR-155 functions as an important mediator in this process. They further show that miR-155 acts to upregulate hexokinase 2 *(hk2)*, through two distinct mechanisms. First, miR-155 promotes *hk2* transcription by activation of signal transducer and activator of transcription 3 (STAT3), a transcriptional activator for *hk2*. Second, via targeting *C/EBP* β (a transcriptional activator for *mir-143*), miR-155 represses *mir-143*, a negative regulator of *hk2*, thus resulting in upregulation of *hk2* expression at the post-transcriptional level. The miR-155-mediated *hk2* upregulation also appears to operate in other types of cancer cells examined. They suggest that the miR-155/miR-143/HK2 axis may represent a common mechanism linking inflammation to the altered metabolism in cancer cells.

参考文献: Jiang et al. (2012) *EMBO J.* 31:1985-998




Model of the dual-switch mechanism through which miR-155 conveys the inflammatory signals to the Warburg effect.

### 重点参考文献

Yin QF*, Yang L*, Zhang Y, Xiang JF, Wu YW, Carmichael GG#, Chen LL# (2012) Long noncoding RNAs with snoRNA ends. *Mol. Cell* [Epub ahead of print]

Du C*, Liu C*, Kang J, Zhao G, Ye Z, Huang S, Li Z, Wu Z, Pei G (2009) MicroRNA miR-326 regulates $T_H$-17 differentiation and is associated with the pathogenesis of multiple sclerosis. *Nat. Immunol.* 10:1252-59

Huang Y, Ji L, Huang Q, Vassylyev DG, Chen X, Ma JB (2009) Structural insights into mechanisms of the small RNA methyltransferase HEN1. *Nature* 461:823-7

Cheng H, Dufu K, Lee CS, Hsu JL, Dias A, Reed R (2006) Human mRNA export machinery recruited to the 5' end of mRNA. *Cell* 127:1389-400

### 延伸参考文献

Wei WJ, Mu SR, Heiner M, Fu X, Cao LJ, Gong XF, Bindereif A, Hui J (2012) YB-1 binds to CAUC motifs and stimulates exon inclusion by enhancing the recruitment of U2AF to weak polypyrimidine tracts. *Nucleic Acids Res.* [Epub ahead of print]

Piao X, Zhang X, Wu L#, Belasco JG# (2010) CCR4-NOT deadenylates mRNA associated with RNA-induced silencing complexes in human cells. *Mol. Cell. Biol.* 30:1486-94

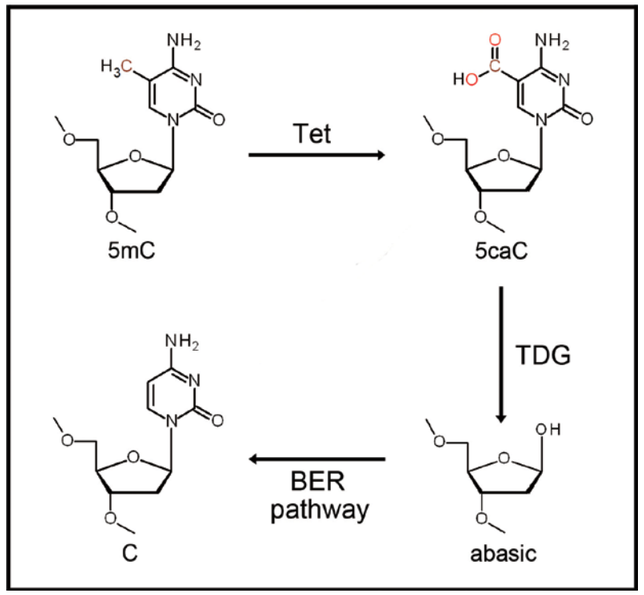




## Tet双加氧酶及胸腺嘧啶DNA糖基化酶介导DNA主动去甲基化
## An active DNA demethylation pathway mediated by Tet and TDG

The prevalent DNA modification in higher organisms is the methylation of cytosine to 5-methylcytosine (5mC), which is partially converted to 5-hydroxymethylcytosine (5hmC) by the Tet (ten eleven translocation) family of dioxygenases. Despite their importance in epigenetic regulation, it is unclear how these cytosine modifications are reversed. Researchers led by Prof. Guoliang Xu demonstrate that 5mC and 5hmC in DNA are oxidized to 5-carboxylcytosine (5caC) by Tet dioxygenases in vitro and in cultured cells. 5caC is specifically recognized and excised by thymine-DNA glycosylase (TDG). Depletion of TDG in mouse embryonic stem cells leads to accumulation of 5caC to a readily detectable level. These data suggest that Tet-mediated oxidation of 5mC followed by TDG-mediated base excision of 5caC constitutes a pathway for active DNA demethylation.

参考文献: He et al. (2011) *Science* 333:1303-07




Model for DNA demethylation promoted by Tet and TDG. Consecutive oxidation of 5mC generates end product-5caC that is recognized and excised by TDG. The resulting abasic site in turn induces the base excision repair pathway, leading to the incorporation of unmethylated cytosines.

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## JARID1B: 一个在前列腺癌中上调的H3K4去甲基化酶
## JARID1B: A H3K4 demethylase upregulated in prostate cancer

Histone methylation is a dynamic process that participates in a diverse array of cellular processes and has been found to associate with cancer. Several histone demethylases have been identified that catalyze the removal of methylation from histone H3 lysine residues. Through bioinformatic and biochemical analysis, researchers led by Prof. Degui Chen identified JARID1B as a H3K4 demethylase. Overexpression of JARID1B resulted in loss of tri-, di-, and monomethyl H3K4 but did not affect other histone lysine methylations. In vitro biochemical experiments demonstrated that JARID1B directly catalyzes the demethylation. The enzymatic activity requires the JmjC domain and uses Fe(II) and α-ketoglutarate as cofactors. Furthermore, they found that JARID1B is up-regulated in prostate cancer tissues, compared with benign prostate samples. They also demonstrated that JARID1B associates with androgen receptor and regulates its transcriptional activity. Thus, they identified JARID1B as a demethylase capable of removing three methyl groups from histone H3 lysine 4 and up-regulated in prostate cancer.

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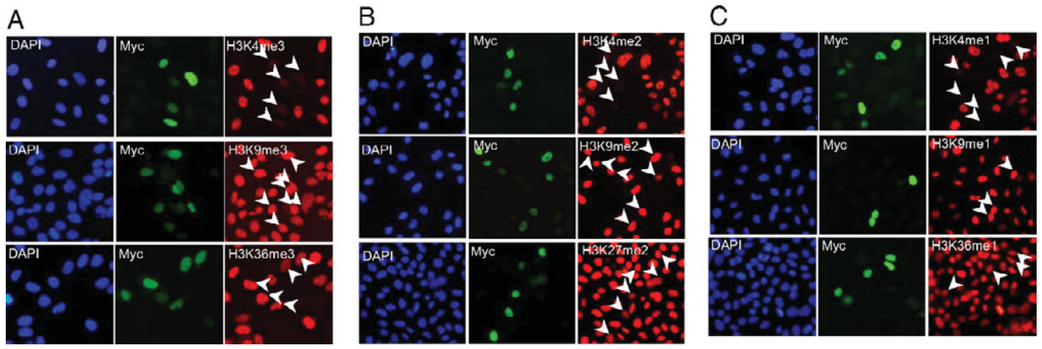


JARID1B removed H3K4 methylation ***in vivo***. HeLa cells transfected with Myc-JARID1B were immunostained with specific antibodies against distinctly methylated lysine residues. (A–C Left) DAPI staining. (A–C Center) Myc staining. (A–C Right) Methylated lysine staining. (A Top) H3K4me3. (A Middle) H3K9me3. (A Bottom) H3K36me3. (B Top) H3K4me2. (B Middle) H3K9me2. (B Bottom) H3K27me2. (C Top) H3K4me1. (C Middle) H3K9me1. (C Bottom) H3K36me1. Arrowheads indicate Myc-JARID1B-expressed cells.

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## 端粒酶亚基Est1p是酵母端粒延长所必需的
## Yeast telomerase subunit Est1p is required for telomere elongation

Telomeres are eukaryotic protein–DNA complexes found at the ends of linear chromosomes that are essential for maintaining genome integrity and are implicated in cellular aging and cancer. The guanine (G)-rich strand of telomeric DNA, usually elongated by the telomerase reverse transcriptase, can form a higher-order structure known as a G-quadruplex *in vitro* and *in vivo*. Several factors that promote or resolve G-quadruplexes have been identified, but the functional importance of these structures for telomere maintenance is not well understood. Researchers led by Prof. Jinqiu Zhou show that the yeast telomerase subunit Est1p, known to be involved in telomerase recruitment to telomeres, can convert single-stranded telomeric G-rich DNA into a G-quadruplex structure in vitro in a $Mg^{2+}$-dependent manner. Cells carrying Est1p mutants deficient in G-quadruplex formation *in vitro* showed gradual telomere shortening and cellular senescence, indicating a positive regulatory role for G-quadruplex in the maintenance of telomere length.

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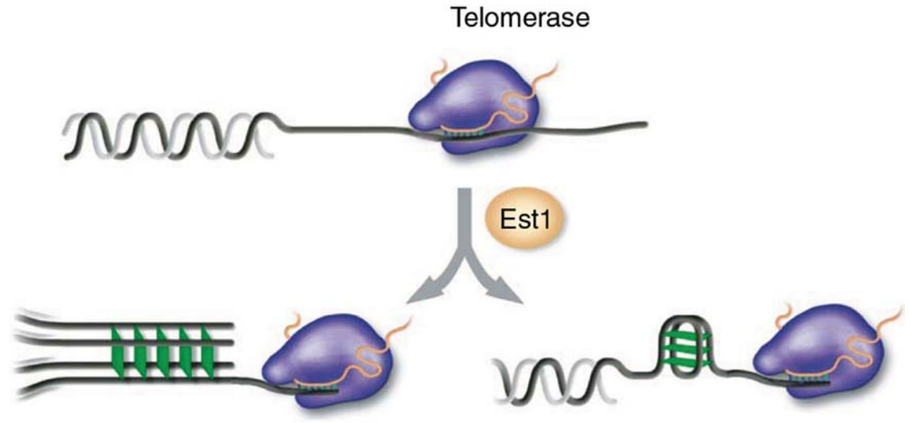


Model of Est1p activating telomere-bound telomerase. Est1p causes telomeric single-stranded DNA to form an intermolecular (left) or an intramolecular (right) G-quadruplex, which translocates or activates Est2p-Tlc1 telomerase.

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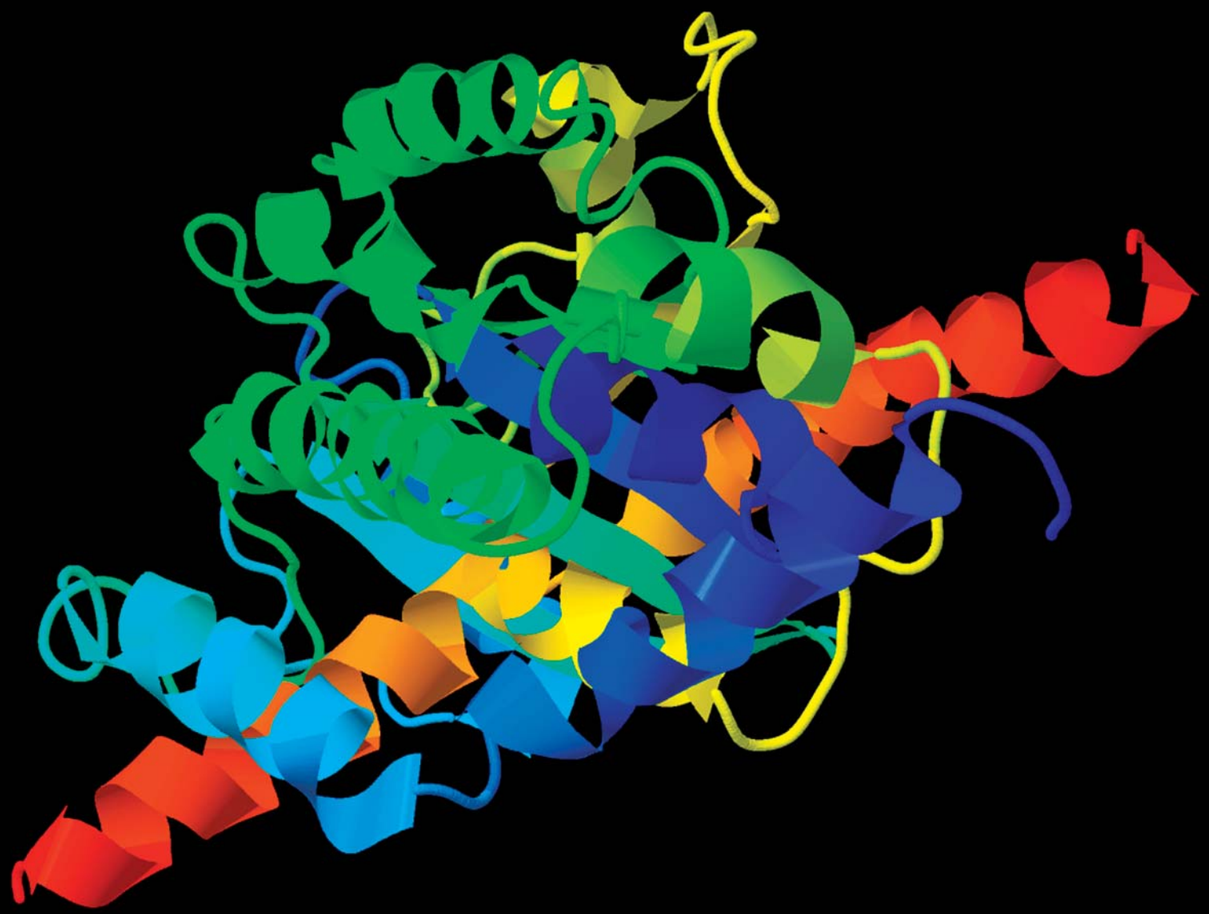


## 科研亮点

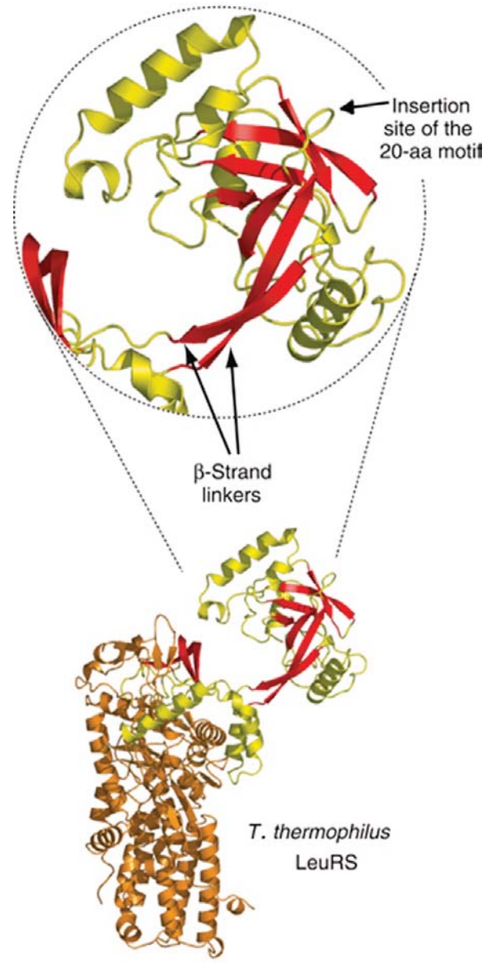
### 蛋白质科学

蛋白质合成与降解
蛋白质结构生物学
蛋白质组学



## 在远古细菌中发现的氨基酰-tRNA合成酶进化遗迹
## Relics of aminoacyl-tRNA synthetase evolution discovered in ancient bacterium

The editing reactions catalyzed by aminoacyl-tRNA synthetases are critical for the faithful protein synthesis by correcting misactivated amino acids and misaminoacylated tRNAs. Researchers led by Prof. Enduo Wang report that the isolated editing domain of leucyl-tRNA synthetase from the deep-rooted bacterium *Aquifex aeolicus* (αβ-LeuRS) catalyzes the hydrolytic editing of both mischarged $tRNA^{Leu}$ and $minihelix^{Leu}$. Within the domain, they have identified a crucial 20-amino-acid peptide that confers editing capacity when transplanted into the inactive *Escherichia coli* LeuRS editing domain. Likewise, fusion of the β-subunit of αβ-LeuRS to the *E. coli* editing domain activates its editing function. These results suggest that αβ-LeuRS still carries the basic features from a primitive synthetase molecule. It has a remarkable capacity to transfer autonomous active modules, which is consistent with the idea that modern synthetases arose after exchange of small idiosyncratic domains. It also has a unique αβ-heterodimeric structure with separated catalytic and tRNA-binding sites. Such an organization supports the tRNA/synthetase coevolution theory that predicts sequential addition of tRNA and synthetase domains.




Overview of the *T. thermophilus* LeuRS and detailed view of its CP1 domain. The lower part of the figure depicts the *T. thermophilus* LeuRS, showing the large size and globular nature of the editing domain. The studied CP1 domain is colored yellow (α-helices and loops) and red (β-strands). The other domains of the molecule are colored orange. The upper part of the figure is a detailed view of the editing domain. The two β-strand linkers that link the editing domain to the catalytic site are indicated, as well as is the insertion point of the crucial '20-aa motif' specific for *A. aeolicus* LeuRS.

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## 结构研究揭示menin调控转录的分子机理
## Structural insights into the mechanism of transcription regulation by menin

Menin is a tumour suppressor protein whose loss or inactivation causes multiple endocrine neoplasia 1 (MEN1), a hereditary autosomal dominant tumour syndrome that is characterized by tumorigenesis in multiple endocrine organs. Menin interacts with many proteins and is involved in a variety of cellular processes. Despite its importance, how menin interacts with many distinct partners and regulates their functions remains poorly understood. Here researchers led by Prof. Ming Lei present the crystal structures of human menin in its free form and in complexes with MLL1 or with JUND, or with an MLL1-LEDGF heterodimer. These structures show that menin contains a deep pocket that binds short peptides of MLL1 or JUND in the same manner, but that it can have opposite effects on transcription. The menin-JUND interaction blocks JUN N-terminal kinase (JNK)-mediated JUND phosphorylation and suppresses JUND-induced transcription. In contrast, menin promotes gene transcription by binding the transcription activator MLL1 through the peptide pocket while still interacting with the chromatin-anchoring protein LEDGF at a distinct surface formed by both menin and MLL1.

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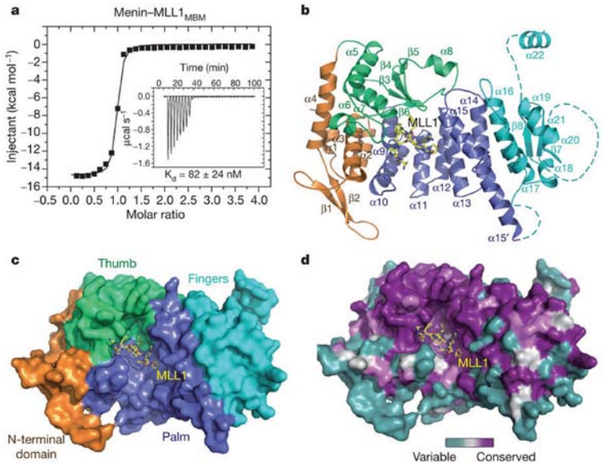


Overview of the human menin–MLL1$_{MBM}$ complex structure. a, Isothermal titration calorimetry measurement of the menin–MLL1$_{MBM}$ interaction. The inset shows the isothermal titration data. b, Overall structure of the menin–MLL1$_{MBM}$ complex. The N-terminal domain is shown in orange, the thumb domain in green, the palm domain in blue, the fingers domain in cyan, and loop regions that are disordered or not included in the crystal structure are shown as dashed lines. MLL1$_{MBM}$ is shown as a stick model in yellow. c, The surface representation of menin indicates that menin adopts a curved left-hand-shaped conformation. d, Front view of the menin–MLL1$_{MBM}$ complex, coloured according to the degree of amino acid conservation among menin homologues.

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## ARL2-GTP-BART晶体结构揭示GTP水解酶与效应蛋白结合新模式
## ARL2-GTP-BART structure reveals a novel mode of GTPase-effector binding

ARL2 is a member of the ADP-ribosylation factor family but has unique biochemical features. BART is an effector of ARL2 that is essential for nuclear retention of STAT3 and may also be involved in mitochondria transport and apoptosis. Researchers led by Prof. Jianping Ding report the crystal structure and biochemical characterization of human ARL2-GTP-BART complex. ARL2-GTP assumes a typical small GTPase fold with a unique N-terminal α helix conformation. BART consists of a six α helix bundle. The interactions between ARL2 and BART involve two interfaces: a conserved N-terminal LLXIL motif of ARL2 is embedded in a hydrophobic cleft of BART and the switch regions of ARL2 interact with helix α3 of BART. Both interfaces are essential for the binding as verified by mutagenesis study. This novel recognition and binding mode is different from that of other small GTPase-effector interactions and provides molecular basis for the high specificity of ARL2 for BART.

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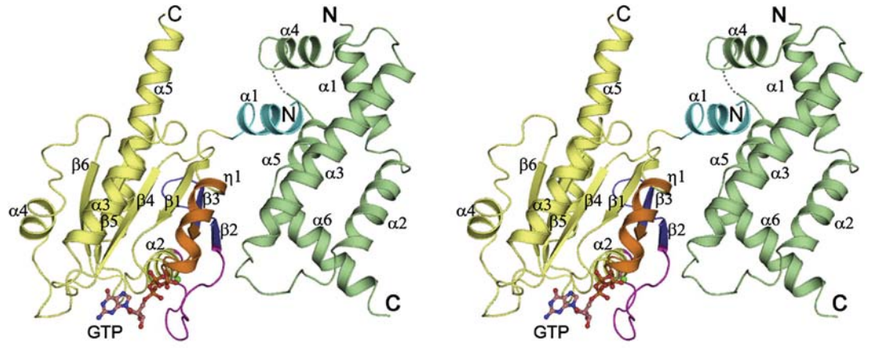


JA stereo view of the ARL2-GTP-BART complex. ARL2 is colored in yellow with the N-terminal α helix in cyan and the switch I, switch II, and inter-switch regions in magenta, orange, and blue, respectively. The bound GTP is shown with a ball-and-stick model and the $Mg^{2+}$ ion in a green sphere. BART is colored in green with the secondary structures labeled.


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## 糖尿病大鼠肝脏线粒体的蛋白质组学分析
## Proteomic characterization of liver mitochondria in diabetic rats

It has been proposed that mitochondrial dysfunction is involved in the pathogenesis of type 2 diabetes (T2D). To dissect the underlying mechanisms, Researchers led by Prof. Rong Zeng performed a multiplexed proteomics study on liver mitochondria isolated from a spontaneous diabetic rat model before/after they were rendered diabetic. Altogether, they identified 1091 mitochondrial proteins, 228 phosphoproteins, and 355 hydroxyproteins. Mitochondrial proteins were found to undergo expression changes in a highly correlated fashion during T2D development. For example, proteins involved in β-oxidation, the tricarboxylic acid cycle, oxidative phosphorylation, and other bioenergetic processes were coordinately up-regulated, indicating that liver cells confronted T2D by increasing energy expenditure and activating pathways that rid themselves of the constitutively increased flux of glucose and lipid. Notably, activation of oxidative phosphorylation was immediately related to the overproduction of reactive oxygen species, which caused oxidative stress within the cells. Increased oxidative stress was also evidenced by our post-translational modification profiles such that mitochondrial proteins were more heavily hydroxylated during T2D development. Moreover, they observed a distinct depression of antiapoptosis and antioxidative stress proteins that might reflect a higher apoptotic index under the diabetic stage. They suggest that such changes in systematic metabolism were causally linked to the development of T2D. Comparing proteomics data against microarray data, they demonstrated that many T2D-related alterations were unidentifiable by either proteomics or genomics approaches alone, underscoring the importance of integrating different approaches. Their compendium could help to unveil pathogenic events in mitochondria leading to T2D and be useful for the discovery of diagnosis biomarker and therapeutic targets of T2D.

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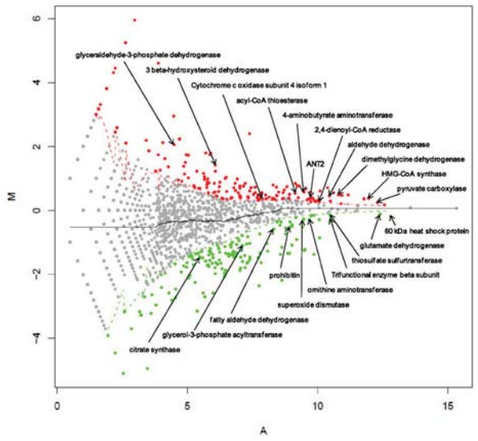


Changes in protein expression level in the early developmental stage of T2D identified by LSPAD. Significantly up-regulated proteins (*p* value <0.01) are in red dots, and down-regulated proteins (*p* value <0.01) are in green. Genes that have already been reported to be associated with T2D are marked.

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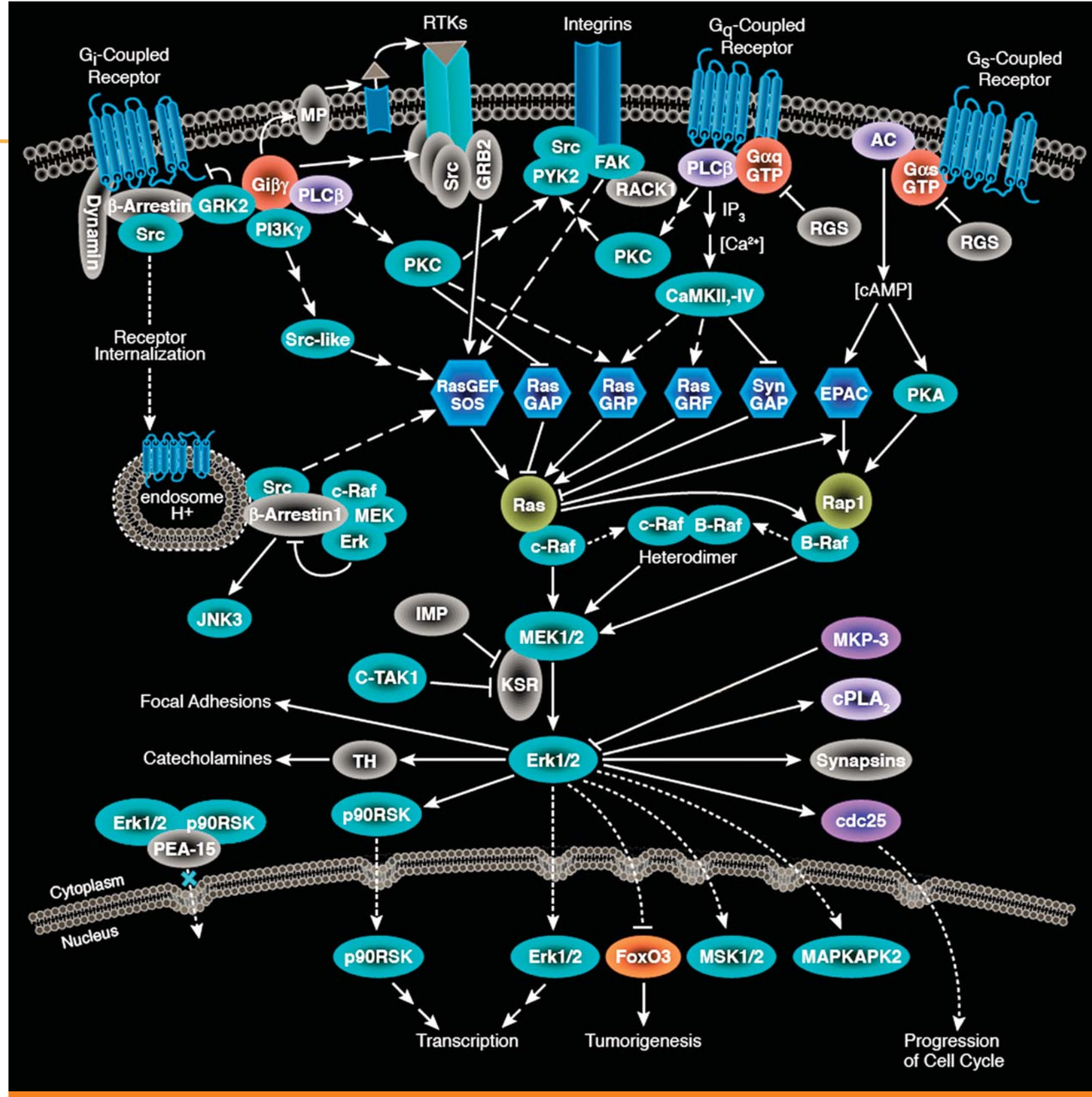


## 科研亮点

### 细胞信号转导

- 免疫信号转导
- GPCR/β-Arrestin信号转导
- Wnt信号转导
- NF-κB信号转导
- TNF-α信号转导

## 细胞外基质蛋白1(ECM1)控制$T_H2$细胞迁出淋巴组织
## ECM1 controls $T_H2$ cell egress from lymph nodes

Type 2 helper T cells ($T_H2$) are critically involved in allergies and asthma. Researchers led by Prof. Bing Sun demonstrate that extracellular matrix protein-1 (ECM1) is highly and selectively expressed in $T_H2$ cells. ECM1 deficiency caused impaired $T_H2$ responses and reduced allergic airway inflammation *in vivo*. Functional analysis demonstrated that although the $T_H2$ polarization of ECM1-deficient cells was unimpaired, these cells had a defect in migration and were retained in peripheral lymphoid organs. This was associated with reduced expression of KLF2 and $S1P_1$. They also found that ECM1 could directly bind the interleukin-2 (IL-2) receptor to inhibit IL-2 signaling and activate $S1P_1$ expression. Their data identify a previously unknown function of ECM1 in regulating $T_H2$ cell migration through control of KLF2 and $S1P_1$ expression.

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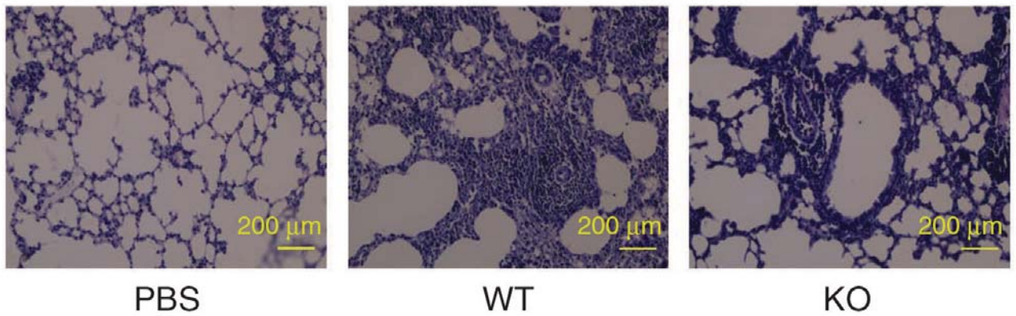


ECM1[BM]-deficient mice show impaired $T_H2$ function owing to defective $T_H2$ cell migration *in vivo*.Wild-type (WT) or *Ecm1*$^{-/-}$bone marrow cells ($1\times10^7$) were transferred into irradiated C57BL/6 mice. Two months later, mice were immunized with OVA and alum and challenged with aerosolized OVA. Mice immunized with PBS served as a negative control. Shown here are lung tissue sections stained with hematoxylin and eosin. Scale bar, 200 μm.

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## 凝血酶受体调控内皮血液转化
## Thrombin receptor regulates endothelial-to-hematopoietic transition

Hematopoietic development and vascular development are closely related physiological processes during vertebrate embryogenesis. Recently, endothelial-to-hematopoietic transition (EHT) was demonstrated to be critical for hematopoietic stem and progenitor cell induction, but its underlying regulatory mechanisms remain poorly understood. Here researchers led by Prof. Gang Pei show that thrombin receptor (F2r), a protease-activated G protein-coupled receptor required for vascular development, functions as a negative regulator during hematopoietic development. F2r is significantly upregulated during hematopoietic differentiation of mouse embryonic stem cells (mESCs) and zebrafish hematopoietic development. Pharmacological or genetic inhibition of F2r promotes hematopoietic differentiation, whereas F2r overexpression shows opposite effects. Further mechanistic studies reveal that F2r-RhoA/ROCK pathway inhibits EHT in vitro and negatively regulates zebrafish EHT and hematopoietic stem cell induction *in vivo*. Taken together, this study demonstrates a fundamental role of F2r-RhoA/ROCK pathway in vertebrate hematopoiesis and EHT, as well as an important molecular mechanism coordinating hematopoietic and vascular development.

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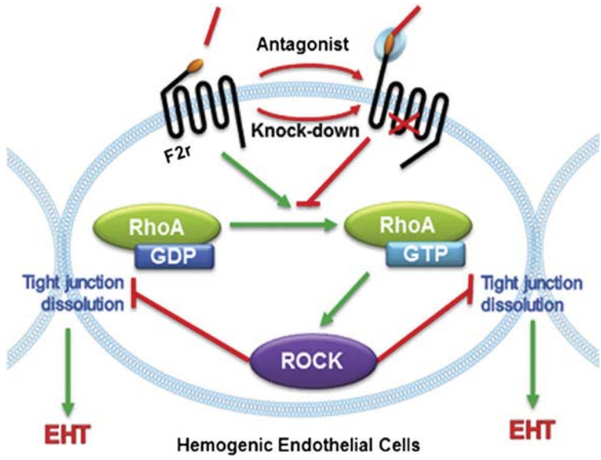


F2r-RhoA/ROCK pathway activation inhibits tight junction dissolution in hemogenic endothelial cells, whereas pharmacological or genetic blockage of F2r reverses the inhibition, accelerating EHT and HSPC induction.

### 重点参考文献

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## H4K20单甲基化介导Wnt靶基因激活
## H4K20 monomethylation mediates Wnt target gene activation

Histone methylation has an important role in transcriptional regulation. However, unlike H3K4 and H3K9 methylation, the role of H4K20 monomethylation (H4K20me-1) in transcriptional regulation remains unclear. Researchers led by Prof. Lin Li show that Wnt3a specifically stimulates H4K20 monomethylation at the T cell factor (TCF)-binding element through the histone methylase SET8. Additionally, SET8 is crucial for activation of the Wnt reporter gene and target genes in both mammalian cells and zebrafish. Furthermore, SET8 interacts with lymphoid enhancing factor-1 (LEF1)/TCF4 directly, and this interaction is regulated by Wnt3a. Therefore, they conclude that SET8 is a Wnt signaling mediator and is recruited by LEF1/TCF4 to regulate the transcription of Wnt-activated genes, possibly through H4K20 monomethylation at the target gene promoters. Their findings also indicate that H4K20me-1 is a marker for gene transcription activation, at least in canonical Wnt signaling.

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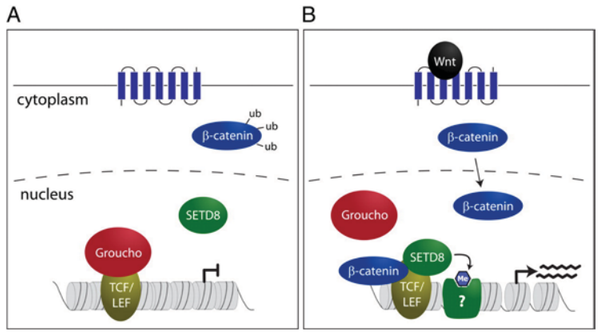


Wnt signaling stimulates SETD8-mediated H4K20me1 at TCF/LEF binding sites (TBEs). (A) In the absence of Wnt ligand, cellular β-catenin is destabilized and cannot enter the nucleus. Wnt target genes are constitutively bound by TCF/LEF transcription factors; however, transcription is blocked by binding of the repressor protein Groucho. (B) Under active Wnt signaling, β-catenin can enter the nucleus and displace Groucho from TCF/LEF. This allows for complex formation with the histone methyltransferase SETD8, which induces H4K20me1 at TBEs. Increased H4K20me1 is a prerequisite for full transcriptional activity of the Wnt target gene, possibly due to recruitment of currently unknown binding proteins. [From Schotta G (2011) *Proc. Natl. Acad. Sci. U S A* 108:3097-8]

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## UXT：一个NF-κB增强体的关键辅助因子
## UXT: An essential cofactor of the NF-κB enhanceosome

As a latent transcription factor, nuclear factor κB (NF-κB) translocates from the cytoplasm into the nucleus upon stimulation and mediates the expression of genes that are important in immunity, inflammation, and development. However, little is known about how it is regulated inside the nucleus. By a two-hybrid approach, researchers led by Prof. Chen Wang identify a prefoldin-like protein, ubiquitously expressed transcript (UXT), that is expressed predominantly and interacts specifically with NF-κB inside the nucleus. RNA interference knockdown of UXT leads to impaired NF-κB activity and dramatically attenuates the expression of NF-κB-dependent genes. This interference also sensitizes cells to apoptosis by tumor necrosis factor-alpha. Furthermore, UXT forms a dynamic complex with NF-κB and is recruited to the NF-κB enhanceosome upon stimulation. Interestingly, the UXT protein level correlates with constitutive NF-κB activity in human prostate cancer cell lines. The presence of NF-κB within the nucleus of stimulated or constitutively active cells is considerably diminished with decreased endogenous UXT levels. Their results reveal that UXT is an integral component of the NF-κB enhanceosome and is essential for its nuclear function, which uncovers a new mechanism of NF-κB regulation.

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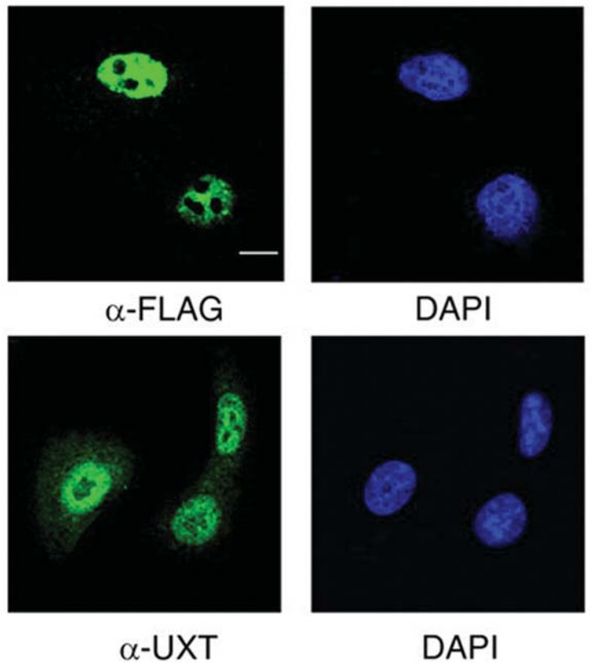


Subcellular localization of endogenous and exogenous UXT. 293T cells were transfected with (top) or without (bottom) FLAG-UXT. Immunofluorescentmicroscopy was performed with the indicated primary antibodies.

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## Miz1降解对于解除Miz1对TNF-α 诱导的JNK激活的抑制作用是必需的
## Miz1 degradation is required for relieving its suppression on TNF-α induced JNK activation

The transcription factor zinc-finger protein Miz1 represses TNF-α–induced JNK activation and the repression is relieved upon TNF-α stimulation. However, the underlying mechanism is incompletely understood. Researchers led by Prof. Anning Lin report that Miz1 interferes with the ubiquitin conjugating enzyme (E2) Ubc13 for binding to the RING domain of TNF-receptor associated factor 2 (TRAF2), thereby inhibiting the ubiquitin ligase (E3) activity of TRAF2 and suppressing TNF-α–induced JNK activation. Upon TNF-α stimulation, Miz1 rapidly undergoes K48-linked polyubiquitination at Lys388 and Lys472 residues and subsequent proteasomal degradation in a TRAF2-dependent manner. Replacement of Lysine 388 and Lysine 472 by arginines generates a nondegradable Miz1 mutant, which significantly suppresses TNF-α–induced JNK1 activation and inflammation. Thus, their results reveal a molecular mechanism by which the repression of TNF-α–induced JNK activation by Miz1 is de-repressed by its own site-specific ubiquitination and degradation, which may account for the temporal control of TNF-α–JNK signaling.

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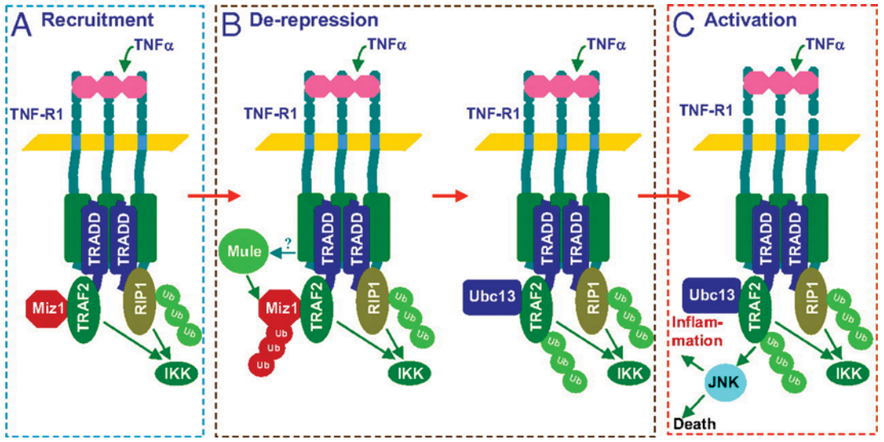


Schematic illustration of the de-repression model by which Miz1 regulates TNF-α–JNK signaling. (A) Upon TNF-α stimulation, Miz1 is recruited to TNF-R1 Complex I in a TRAF2-dependent manner and blocks immediate K63-linked polyubiquitination of TRAF2, so that TRAF2 and ubiquitinated receptor interacting protein 1 (RIP1) activate IKK but not JNK. (B) TNF-α induces Miz1 K48-linked polyubiquitination, which is catalyzed by Mule, and proteasomal degra-dation, so that Ubc13 can bind to TRAF2 and promote TRAF2 K63-linked polyubiquitination. (C) Polyubiquitinated TRAF2 activates JNK, which contributes to inflammation or cell death, when NF-κB activation is impaired.

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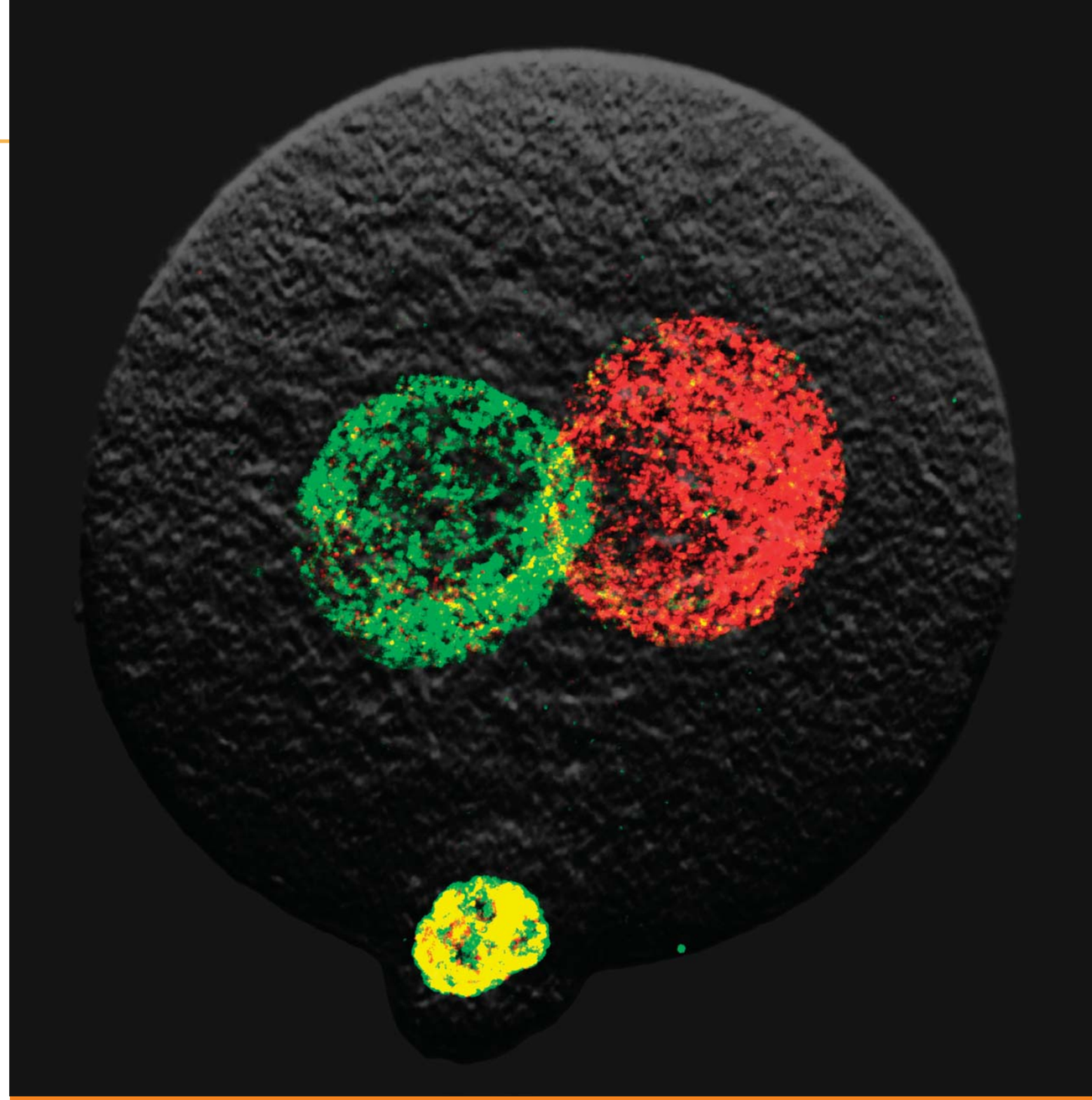

## 科研亮点

### 细胞与干细胞生物学

运动与凋亡
分化与发育
干细胞生物学
生殖生物学
神经生物学

## 小分子RNA miR-129-3p通过调控CP110和肌动蛋白动态来控制纤毛组装
## miR-129-3p controls cilia assembly by regulating CP110 and actin dynamics

Ciliogenesis requires the removal of CP110 from the mother centriole; actin dynamics also influence ciliation, at least partly by affecting the centrosomal accumulation of ciliogenic membrane vesicles. How these distinct processes are properly regulated remains unknown. Researchers led by Prof. Xueliang Zhu show that miR-129-3p, a microRNA conserved in vertebrates, controlled cilia biogenesis in cultured cells by concomitantly down-regulating CP110 and repressing the branched F-actin formation. Blocking miR-129-3p inhibited serum starvation-induced ciliogenesis, whereas its overexpression potently induced ciliation in proliferating cells and also promoted cilia elongation. Gene expression analysis further identified Arp2, Toca1, abLIM1 and abLIM3 as its targets in ciliation-related actin dynamics. Moreover, its inhibition in zebrafish embryos suppressed ciliation in the Kupffer's vesicle and the pronephros, and induced developmental abnormalities including a curved body, pericardial oedema, and defective left-right asymmetry. Therefore, their results reveal a mechanism that orchestrates both the centriole-to-basal body transition and subsequent cilia assembly via microRNA-mediated post-transcriptional regulation.

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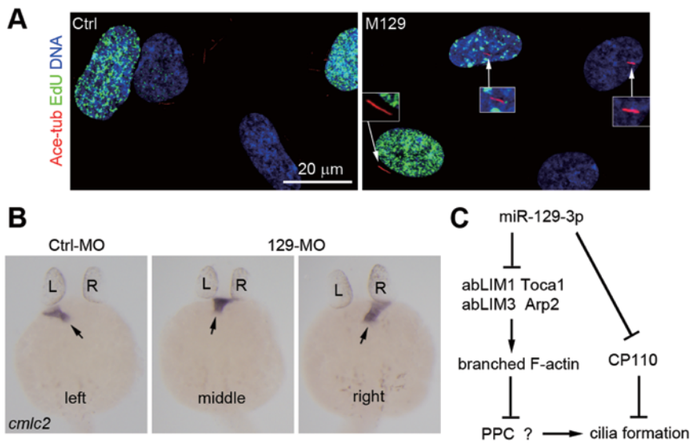


(A) Overexpression of miR-129-3p (M129) induced ciliogenesis in cycling interphase cells. Acetylated tubulin (Ace-tub) was used as a cilia marker. EdU-positive cells are in S or G2 phase. (B) Inhibition of miR-129-3p (129-MO) in zebrafish induced defects in the left-right asymmetry. (C) Model for the functions of miR-129-3p in cilia formation. miR-129-3p controlled cilia biogenesis in cultured cells by concomitantly downregulating CP110 and repressing the branched F-actin formation.

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## LKB1在胸腺细胞发育中起关键作用
## LKB1 plays a critical role in thymocyte development

The serine/threonine kinase LKB1 is a tumour suppressor that regulates cell growth, polarity, and proliferation in many different cell types. It was previously demonstrated that LKB1 controls thymocyte survival via regulation of AMPK activation. Researchers led by Prof. Xiaolong Liu show that LKB1 was also involved in thymocyte positive selection through regulation of T cell receptor (TCR) signalling. Both Lck-Cre- and CD4-Cre-mediated deletion of LKB1 impaired the generation of mature CD4 and CD8 single positive (SP) thymocytes that might have resulted from the attenuated tyrosine phosphorylation of phospholipase C-γ 1 (PLCγ1) in the absence of LKB1. They found that LKB1 was directly phosphorylated by Lck at tyrosine residues 36, 261, and 365 and predominately interacted with LAT and PLCγ1 following TCR stimulation. Loss of LKB1 led to impaired recruitment of PLCγ1 to the LAT signalosome. Correlatively, LKB1-deficient thymocytes failed to upregulate lineage-specifying factors, and to differentiate into SP thymocytes even if their impaired survival was rescued. These observations indicated that LKB1 is a critical component involved in TCR signalling, and their studies provide novel insights into the mechanisms of LKB1-mediated thymocyte development.

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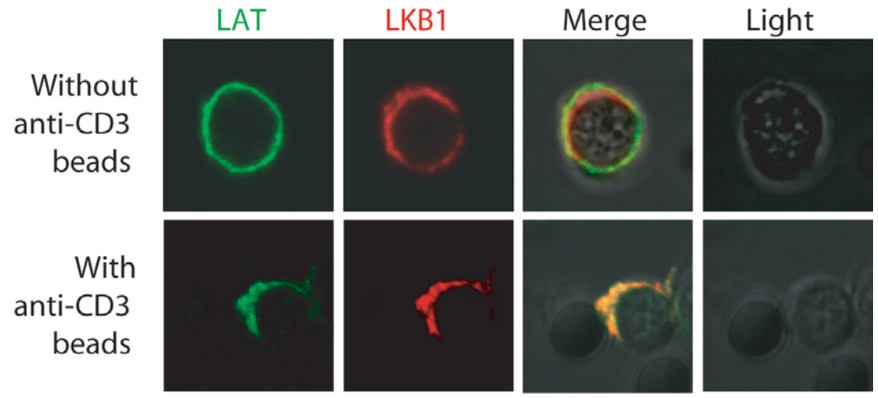


Colocalization of LKB1 with LAT upon TCR stimulation. Sorted T lymphocytes were incubated with anti-CD3-coated Dynabeads, stained with anti-LAT and anti-LKB1 antibodies and imaged using confocal microscopy (magnification, × 630). Images are representative of 99/100 (control) or 90/100 (stimulated) counted cells.

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## 直接将小鼠成纤维细胞转分化为功能性肝细胞样细胞
## Direct conversion of mouse fibroblasts to functional hepatocyte-like cells

The generation of functional hepatocytes independent of donor liver organs is of great therapeutic interest with regard to regenerative medicine and possible cures for liver disease. Induced hepatic differentiation has been achieved previously using embryonic stem cells or induced pluripotent stem cells. Particularly, hepatocytes generated from a patient's own induced pluripotent stem cells could theoretically avoid immunological rejection. However, the induction of hepatocytes from induced pluripotent stem cells is a complicated process that would probably be replaced with the arrival of improved technology. Overexpression of lineage-specific transcription factors directly converts terminally differentiated cells into some other lineages, including neurons, cardiomyocytes and blood progenitors; however, it remains unclear whether these lineage-converted cells could repair damaged tissues *in vivo*. Researchers led by Prof. Lijian Hui demonstrate the direct induction of functional hepatocyte-like (iHep) cells from mouse tail-tip fibroblasts by transduction of Gata4, Hnf1α and Foxa3, and inactivation of $p19^{Arf}$. iHep cells show typical epithelial morphology, express hepatic genes and acquire hepatocyte functions. Notably, transplanted iHep cells repopulate the livers of fumarylacetoacetate-hydrolase-deficient ($Fah^{-/-}$) mice and rescue almost half of recipients from death by restoring liver functions. Their study provides a novel strategy to generate functional hepatocyte-like cells for the purpose of liver engineering and regenerative medicine.

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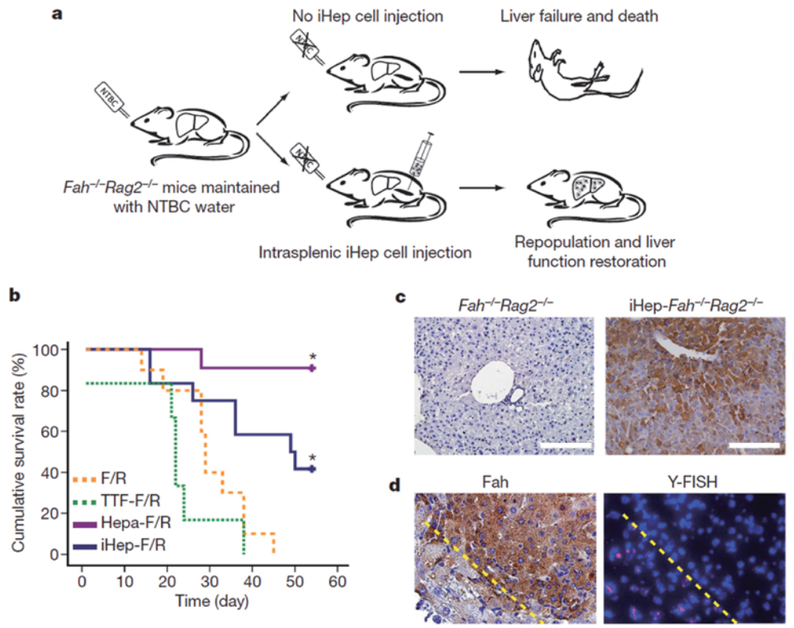


iHep cell transplantation rescues Fah-deficient mice. (a) Schematic outline of iHep cell transplantation into livers of $Fah^{-/-}Rag2^{-/-}$ mice. (b) Kaplan–Meier survival curve of primary-hepatocyte-transplanted $Fah^{-/-}Rag2^{-/-}$ mice (Hepa-F/R, $n$ = 10), iHep-cell-transplanted $Fah^{-/-}Rag2^{-/-}$ mice (iHep-F/R, $n$ = 12), TTF-transplanted $Fah^{-/-}Rag2^{-/-}$ mice (TTF-F/R, $n$ = 6) and control $Fah^{-/-}Rag2^{-/-}$ mice (F/R, $n$ = 10) after NTBC withdrawal. *, $P < 0.02$, log-rank test. (c) Repopulation of iHep cells in $Fah^{-/-}Rag2^{-/-}$ livers was determined by Fah immunostaining (brown cytoplasmic staining). (d) Female iHep cells were transplanted into male $Fah^{-/-}Rag2^{-/-}$ livers. Serial liver sections were stained for both Fah immunostaining and Y-chromosome FISH staining (red dots). The boundary of the $Fah^{+}$ nodule is indicated by a dashed yellow line.





## 孤雄单倍体胚胎干细胞：一种潜在的精子替代物
## Androgenetic haploid embryonic stem cells: a potential sperm replacement

Haploid cells are amenable for genetic analysis. Recent success in the derivation of mouse haploid embryonic stem cells (haESCs) via parthenogenesis has enabled genetic screening in mammalian cells. However, successful generation of live animals from these haESCs, which is needed to extend the genetic analysis to the organism level, has not been achieved. Researchers led by Prof. Jinsong Li and Prof. Guoliang Xu report the derivation of haESCs from androgenetic blastocysts. These cells, designated as AG-haESCs, partially maintain paternal imprints, express classical ESC pluripotency markers, and contribute to various tissues, including the germline, upon injection into diploid blastocysts. Strikingly, live mice can be obtained upon injection of AG-haESCs into MII oocytes, and these mice bear haESC-carried genetic traits and develop into fertile adults. Furthermore, gene targeting via homologous recombination is feasible in the AG-haESCs. Their results demonstrate that AG-haESCs can be used as a genetically tractable fertilization agent for the production of live animals via injection into oocytes.

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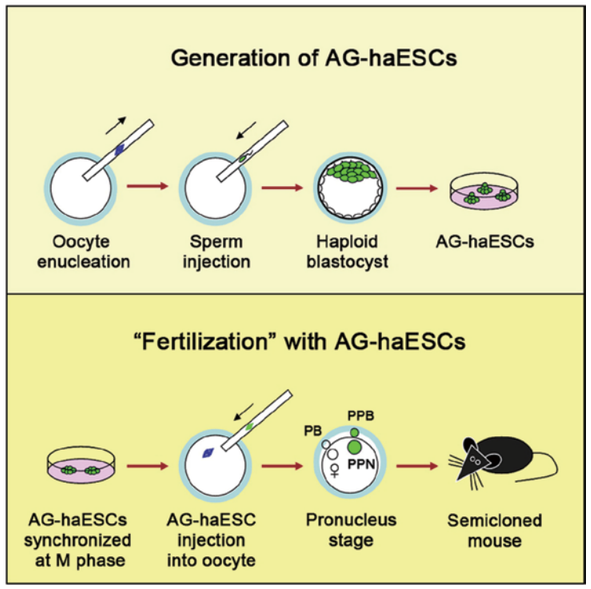


Diagram showing the generation of AG-haESCs (top) and "fertilization" of oocytes with AG-haESCs (bottom).

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## 首个全基因组雄激素受体结合位点图谱
## The first genome-wide mapping of androgen receptor binding sites

Epididymal function depends on androgen signaling through the androgen receptor (AR), although most of the direct AR target genes in epididymis remain unknown. Researchers led by Prof. Yonglian Zhang globally mapped the AR binding regions in mouse caput epididymis in which AR is highly expressed. Chromatin immunoprecipitation sequencing indicated that AR bound selectively to 19,377 DNA regions, the majority of which were intergenic and intronic. Motif analysis showed that 94% of the AR binding regions harbored consensus androgen response elements enriched with multiple bindihuing motifs that included nuclear factor 1 and activator protein 2 sites consistent with combinatorial regulation. Unexpectedly, AR binding regions showed limited conservation across species, regardless of whether the metric for conservation was based on local sequence similarity or the presence of consensus androgen response elements. Further analysis suggested the AR target genes are involved in diverse biological themes that include lipid metabolism and sperm maturation. Potential novel mechanisms of AR regulation were revealed at individual genes such as cysteine-rich secretory protein 1. The composite studies provide new insights into AR regulation under physiological conditions and a global resource of AR binding sites in a normal androgen-responsive tissue.

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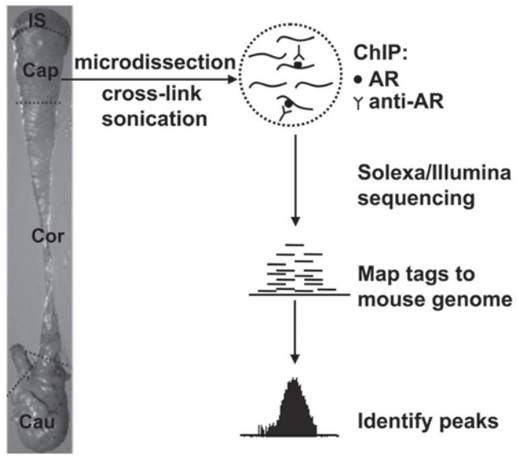


Overview of the ChIP-seq approach and validation of AR-binding sites identified by ChIP-seq. Tissue dissection boundaries are indicated for adult mouse epididymis. IS, Initial segment; Cap, caput; Cor, corpus; Cau, cauda. Caput (Cap) epididymides were pooled from six mice and ChIP-seq was performed using an AR antibody. Tags that uniquely aligned to the reference mouse genome were used to define the peaks.

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## Smad6通过抑制Wnt信号转导促进神经元分化
## Smad6 promotes neuronal differentiation by inibiting Wnt signaling

Proliferation of the neural/neuronal progenitor cells (NPCs) at the ventricular zone of the dorsal spinal cord requires the stimuli of Wnt and bone morphogenic protein (BMP). However, how these two signaling pathways are regulated to initiate differentiation in the NPCs as they enter the intermediate zone is not known. Researchers led by Prof. Naihe Jing show that Smad6, a negative regulator of BMP signaling, is expressed in the intermediate zone of the chick dorsal spinal cord. Knockdown experiments show that Smad6 is required for promoting NPCs to exit the cell cycle and differentiate into neurons. Although they find that Smad6 inhibits BMP signaling, as expected, they also find that Smad6 unexpectedly inhibits the Wnt/β-catenin pathway. The inhibition of the Wnt/β-catenin pathway by Smad6 is independent of its effect on the BMP pathway. Rather, Smad6 through its N-terminal domain and link region enhances the interaction of C-terminal binding protein with the β-catenin/T cell factor (TCF) complex and the TCF-binding element to inhibit β-catenin–mediated transcriptional activation. Their study provides evidence that transition of NPCs from a proliferative state to a differentiating state is controlled by the dual inhibitory role of Smad6 to both BMP and Wnt signaling at the level of transcription.

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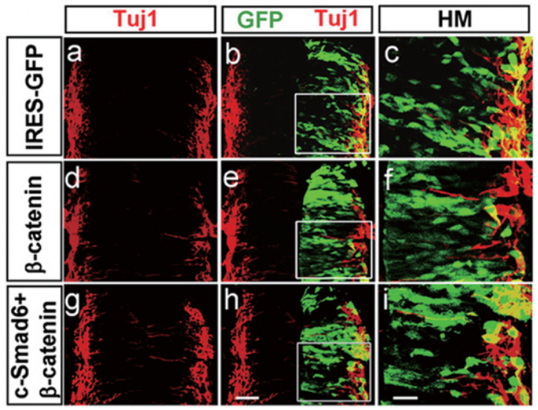


Smad6 promotes neuronal differentiation by inhibiting the Wnt/β-catenin pathway. Shown here are the images of electroporated chick spinal cords. The boxed regions in *b, e,* and *h* are shown at higher magnification in *c, f,* and *i*, respectively. Dorsal is to the top for all sections. (*Scale bars:* 50 μm for h; 25 μm for i.

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## 科研亮点

### 癌症和其它重大疾病

癌症生物学
癌症分子医学
代谢性疾病
神经退行性疾病
肝脏疾病



## 赖氨酰氧化酶(LOX)介导的细胞外基质重构参与肺癌发展过程
## LOX-mediated extracellular matrix remodeling contributes to lung cancer progression

LKB1 loss-of-function mutations, observed in ~30% of human lung adenocarcinomas, contribute significantly to lung cancer malignancy progression. Researchers led by Prof. Gaoxiang Ge and Prof. Hongbin Ji show that lysyl oxidase (LOX), negatively regulated by LKB1 through mTOR-HIF-1α signaling axis, mediates lung cancer progression. Inhibition of LOX activity dramatically alleviates lung cancer malignancy progression. Up-regulated LOX expression triggers excess collagen deposition in *Lkb1*-deficient lung tumors, and thereafter results in enhanced cancer cell proliferation and invasiveness through activation of β1 integrin signaling. High LOX level and activity correlate with poor prognosis and metastasis. Their findings provide evidence of how LKB1 loss of function promotes lung cancer malignancy through remodeling of extracellular matrix microenvironment, and identify LOX as a potential target for disease treatment in lung cancer patients.

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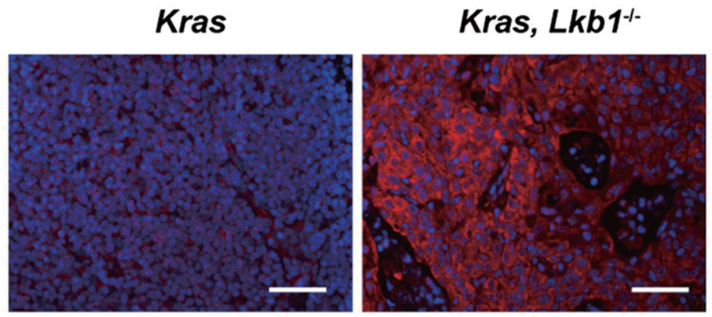


LKB1 down-regulates LOX in lung cancer. Shown here is LOX immunofluorescent staining on *Kras* and *Kras/Lkb1*$^{-/-}$ lung tumor sections. (Scale bars: 100 μm.)

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## TAT-LPTS-LC：一个潜在的蛋白质抗癌药物
## TAT-LPTS-LC: A potential protein-based anticancer agent

Human *liver-related putative tumor suppressor (LPTS)* is a gene that encodes a telomerase inhibitory protein that is similar to human Pin2/TRF1-interacting protein. The LPTS protein binds directly to the telomerase catalytic subunit (human telomerase reverse transcriptase) and suppresses telomerase activity. Telomere maintenance and telomerase activity are required for long-term proliferation of cancer cells, so LPTS might be used in anticancer strategies.In a study conducted by researchers led by Prof. Mujun Zhao, the purified TAT–LPTS-LC protein was efficiently delivered into the cells, where it suppressed telomerase activity and shortened telomere length. TAT–LPTS-LC inhibited proliferation of telomerase-positive hepatocellular carcinoma BEL-7404 and hepatoblastoma HepG2cells and induced their death; however, it had no effect on telomerase-negative liver cell line L02 and osteosarcoma cell line Saos-2. In mice, tumor formations by BEL-7404 cells were suppressed by TAT-LPTS-LC treatments. Transduction of hepatoma cells with a fusion protein that contains the C-terminal, functional fragment of LPTS and human immunodeficiency virus Tat (TAT–LPTS-LC) causes telomere shortening, limits proliferation, and inhibits growth of tumors from these cells in mice. TAT–LPTS-LC inhibits telomerase activity and might be developed as an anticancer agent.

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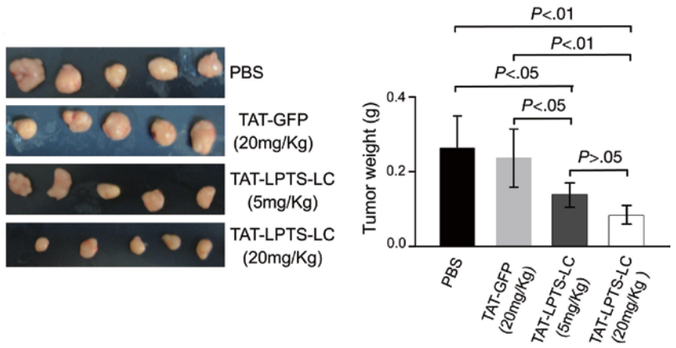


TAT-LPTS-LC suppresses the xenograft growth of BEL-7404 cells in nude mice. At 7 weeks after xenografting, the tumors were removed and photographed. The average tumor weights were counted. Statistical significance was set at a *P* value of less than .05.

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## 白桦脂醇(Betulin)：一个高脂血症药物开发的潜在先导化合物
## Betulin: A potential leading compound for hyperlipidemia drug development

Sterol regulatory element-binding proteins (SREBPs) are major transcription factors activating the expression of genes involved in biosynthesis of cholesterol, fatty acid and triglyceride. Researchers led by Prof. Baoliang Song identified a small molecule, betulin, that specifically inhibited the maturation of SREBP by inducing interaction of SREBP cleavage activating protein (SCAP) and Insig. Inhibition of SREBP by betulin decreased the biosynthesis of cholesterol and fatty acid. In vivo, betulin ameliorated diet-induced obesity, decreased the lipid contents in serum and tissues, and increased insulin sensitivity. Furthermore, betulin reduced the size and improved the stability of atherosclerotic plaques. Their study demonstrates that inhibition SREBP pathway can be employed as a therapeutic strategy to treat metabolic diseases including type II diabetes and atherosclerosis. Betulin, which is abundant in birch bark, could be a leading compound for development of drugs for hyperlipidemia.

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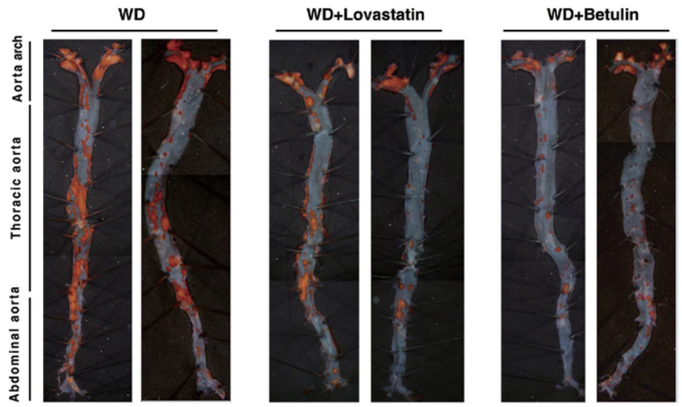


Treatment of betulin decreases atherosclerosis in *LDLR*$^{-/-}$ mice. Eight-week-old male *LDLR*$^{-/-}$ mice were randomly grouped and fed with WD supplemented with vehicle (n = 7), 30 mg/kg/day of lovastatin (n = 3), or 30 mg/kg/day of betulin (n = 6) for 14 weeks. Blood samples were collected 3 days before the end of treatment and centrifugalized for serum. At the end of experiment, the aorta and liver were isolated for further analysis. WD, western-type diet. Shown here are representative photographs from en face analysis of aortas from different groups after 14 week treatment.

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## $\beta_2$-肾上腺素能受体的非正常激活参与阿尔兹海默氏症发病过程
## Abnormal activation of $\beta_2$-AR may contribute to Alzheimer disease pathogenesis

Amyloid plaque is the hallmark and primary cause of Alzheimer disease. Mutations of presenilin-1, the γ-secretase catalytic subunit, can affect amyloid-β (Aβ) production and Alzheimer disease pathogenesis. However, it is largely unknown whether and how γ-secretase activity and amyloid plaque formation are regulated by environmental factors such as stress, which is mediated by receptors including $\beta_2$-adrenergic receptor ($\beta_2$-AR). Researchers led by Prof. Gang Pei show that activation of $\beta_2$-AR enhanced γ-secretase activity and thus Aβ production. This enhancement involved the association of $\beta_2$-AR with presenilin-1 and required agonist-induced endocytosis of $\beta_2$-AR and subsequent trafficking of γ-secretase to late endosomes and lysosomes, where Aβ production was elevated. Similar effects were observed after activation of δ-opioid receptor. Furthermore, chronic treatment with $\beta_2$-AR agonists increased cerebral amyloid plaques in an Alzheimer disease mouse model. Thus, $\beta_2$-AR activation can stimulate γ-secretase activity and amyloid plaque formation, which suggests that abnormal activation of $\beta_2$-AR might contribute to Aβ accumulation in Alzheimer disease pathogenesis.

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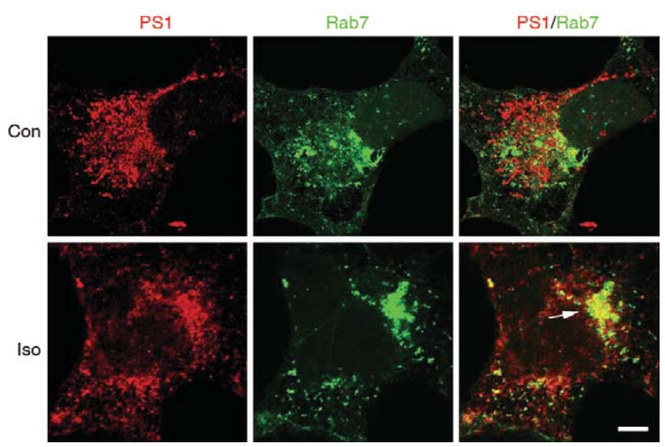


Increased γ-secretase and Aβ in endocytic compartments. Shown here is an immunofluorescence assay analyzing the colocalization of PS1 (red) and GFP-Rab7 (green) after 30 min of isoproterenol treatment. Arrow, punctal structure containing PS1 and GFP-Rab7. Scale bar, 8 μm. IP, immunoprecipitation.

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## Cdc42在肝脏再生过程中调控增殖信号转导
## Cdc42 regulates proliferative signaling during liver regeneration

Cdc42, a member of the Rho guanosine triphosphatase (GTPase) family, plays important roles in the regulation of the cytoskeleton, cell proliferation, cell polarity, and cellular transport, but little is known about its specific function in mammalian liver. Researchers led by Prof. Zhengjun Chen investigated the function of Cdc42 in regulating liver regeneration. Using a mouse model with liver-specific knockout of Cdc42 (Cdc42LK), they studied liver regeneration after partial hepatectomy. Histological analysis, immunostaining, and western blot analysis were performed to characterize Cdc42LK livers and to explore the role of Cdc42 in liver regeneration. In control mouse livers, Cdc42 became activated between 3 and 24 hours after partial hepatectomy. Loss of Cdc42 led to a significant delay of liver recovery after partial hepatectomy, which was associated with reduced and delayed DNA synthesis indicated by 5-bromo-2'-deoxyuridine staining. Consistent with this, expression of cyclins D1, A, and E was markedly delayed or reduced in Cdc42LK livers during regeneration. As a potential effector of Cdc42, Rac1 activation was dramatically attenuated in Cdc42LK livers after partial hepatectomy, suggesting it is regulated in a Cdc42-dependent manner. Activation of certain proliferative signaling pathways, such as extracellular signal–regulated kinase, c-Jun N-terminal kinase, and p70S6 kinase pathways, was delayed in Cdc42LK livers. In addition, dilated bile canaliculi and excessive lipid accumulation were observed in mutant livers during liver regeneration, which may result from impaired cytoskeletal organization and intracellular trafficking in hepatocytes. In summary, their results revealed important roles of Cdc42 in the regulation of proliferative signaling during liver regeneration.

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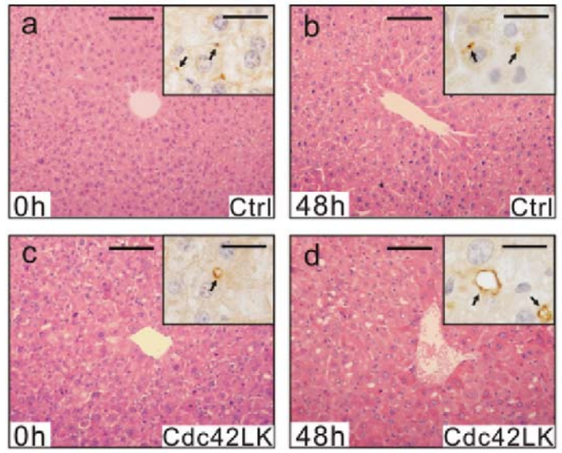


Histological analysis of mice livers during regeneration. Hematoxylin-eosin stained liver sections at (a, c) 0 hours and (b, d) 48 hours after PH. Dilated bile canaliculi in Cdc42LK livers were apparent before hepatectomy and became more obvious at 48 hours revealed by multidrug resistance protein 2 staining (arrows in each inset). Low power scale bars: 100 μm, insets: 20 μm.

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## 知识产权

2009 - 2011 年，研究所申请专利 102 件，获授权 54 件，其中国际专利申请 14 件，获授权 5 件。

## 国际专利(2009-2011)

| 专利号 | 专利名称 | 授权日期 | 发明人 |
|---|---|---|---|
| EP 1364963 B1 | A novel natural antibacterial peptide, the nucleotide sequence encoding it and the use thereof | 2011.3.9 | Yonglian Zhang, Hsiaochang Chan, Peng Li, Bin He, Siucheung So, Yiuwa Chung, Quan Shang |
| US 7939497 B2 | Detection and modulation of Slit and Roundabount(robo)mediated angio-genesis and uses thereof | 2011.5.10 | Jianguo Geng |
| US 8026073 B2 | A G protein coupled receptor antagonist and its use for preventing and treating Alzheimer's disease | 2011.9.27 | Ganng Pei, Yanxiang Ni, Xiaohui Zhao |
| US 8030015 B2 | Tumor-inhibiting protein and the use thereof | 2011.10.4 | Mujun Zhao, Zhenhua Xu, Liang Liang, Zaiping Li |
| US 7741468 B2 | Human liver regeneration associated protein and the use thereof | 2010.6.22 | Mujun Zhao, Zhanwu Liu, Jie Qiu, Zaiping Li |





## 转移转化

2009 - 2011 年，研究所与国内企业签订专利许可合同 6 个，合同金额 41,686 万元，到帐 81 万元。

2010 年，生化与细胞所科研人员发明的“检测和控制由 Slit2 与 Robo 相互作用而导致的血管增生及其用途”，给予 Sanofi-Aventis 公司美国和欧洲专利及其相关技术秘密的独占使用权，合同总金额约 6,100 万美元，外加销售额提成。

2009 - 2011 年，生化与细胞所与国内企业开展合作研究、技术转让、委托研究 7 项，合同金额 1028 万元，到帐 145 万元．签订技术服务合同 12 个，合同金额 369 万元，到帐 344 万元。

2011 年，研究所与山东益康药业有限公司确立了合作关系，由企业投资，利用研究所的基础研究成果，双方联合研发具有自主知识产权的国家一类生物医药 EFE-6。



2009 年，生化与细胞所与徐汇区中心医院共建癌症研究中心，开展转化型癌症研究。在此基础上，2012 年以来，生化与细胞所正与东方肝胆医院合作共建癌症研究中心。此外 ,研究所与上海市肺科医院、上海市胸科医院、上海市肿瘤医院、上海市新华医院也建立了密切的合作关系。

# 主办期刊


## Cell Research

主编

裴　钢 研究员

简介

Cell Research(《细胞研究》) 创刊于 1990 年 ,是由生化与细胞所主办的、《自然》出版集团出版的 SCI 收录国际学术月刊。Cell Resarch 2011 年影响因子达到 8.190，在 180 种 SCI 收录的细胞生物学领域期刊中排名第 23 位，在 154 种 SCI 收录的中国期刊中排名第 1 位。

网站

http://www.cell-research.com/

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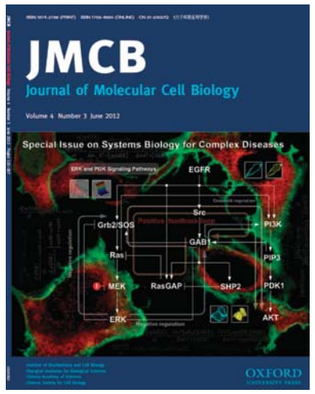


## Journal of Molecular Cell Biology

主编

吴家睿 研究员

简介

Journal of Molecular Cell Biology (《分子细胞生物学报》) 创刊于 2009 年，是由生化与细胞所参与主办的、牛津大学出版社出版的 SCI 收录在线国际学术双月刊。JMCB 2011 年影响因子达到 7.667，在 180 种 SCI 收录的细胞生物学领域期刊中排名第 28 位。

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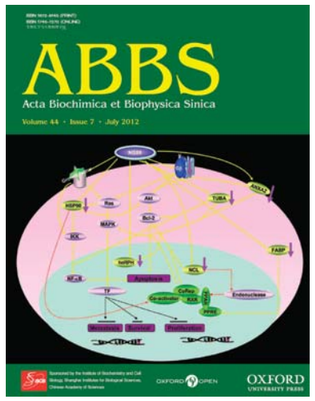


## Acta Biochimica et Biophysica Sinica

主编

李伯良 研究员

简介

Acta Biochimica et Biophysica Sinica (《生物化学与生物物理学报》) 创刊于 1958 年，是由生化与细胞所主办的、牛津大学出版社出版的 SCI 收录国际学术月刊。ABBS 2011 年影响因子为 1.376。

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行政楼前的小枫树

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1987 年成立的分子生物学国家重点实验室是我国在生命科学研究领域设立的第一个国家重点实验室。实验室紧密结合“人口与健康”国家重大需求，定位于创新性基础研究，旨在跻身于分子生物学领域国际最前沿，并为防治人类重大疾病作出重要贡献。

李　林

实验室主任

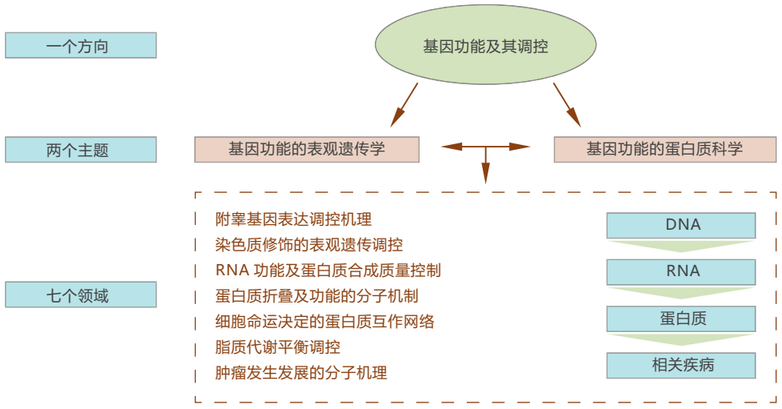
中科院院士

施蕴渝

学术委员会主任

中科院院士

## 学术布局




## 人才队伍

研究组长 29 人，包括中科院院士 5 人，“千人”2 人，“杰青”7 人，“百人”15 人。

## 论文发表

2009-2011 年，实验室共发表 SCI 论文 148 篇，其中 IF≥5 的 81 篇，IF≥10 的 11 篇，篇均 IF 为 7.3。

## 专利申请

2009-2011 年，实验室共申请专利 28 项，授权专利 20 项。

## 奖励荣誉

成果“揭示 Tet 双加氧酶在哺乳动物表观遗传调控中的重要作用”入选 2011 年“中国科学十大进展”。



# 细胞生物学国家重点实验室

2011 年 10 月，获科技部立项批准，研究所在原中科院分子细胞生物学重点实验室（成立于 1997 年）基础上筹建细胞生物学国家重点实验室，筹建期两年。实验室以成为国际一流的细胞生物学研究单元为目标，力争持续性地作出高水平的基础和应用基础研究发现，为“人口与健康”国家重大需求提供源头创新性成果和技术支撑。

朱学良

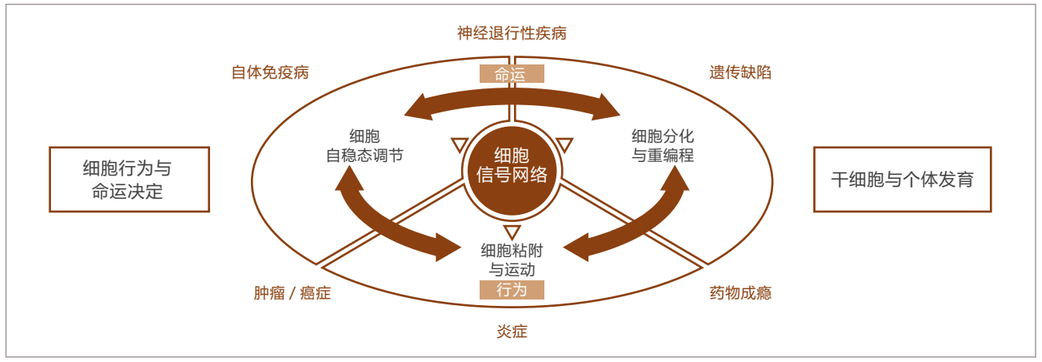
实验室主任

王红阳

学术委员会主任

工程院院士

## 学术布局




## 人才队伍

研究组长 28 人，包括中科院院士 3 人，“千人”1 人，“杰青”8 人，“百人”19 人。

## 论文发表

2009-2011 年，实验室共发表 SCI 论文 118 篇，其中 IF≥5 的 79 篇，IF≥10 的 17 篇，篇均 IF 为 7.8。

## 专利申请

2009-2011 年，实验室共申请专利 48 项，授权专利 18 项。

## 奖励荣誉

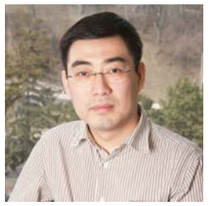
成果“将小鼠成纤维细胞成功转化为功能性肝细胞样细胞”入选 2011 年“中国科学十大进展”，成果“发现β- 抑制因子 -2 复合体信号缺损可导致胰岛素耐受”入选 2009 年“中国基础研究十大新闻”。

# 国家蛋白质科学综合研究中心(上海)

国家蛋白质科学综合研究中心（上海）(以下简称“蛋白质中心”）是依托于国家蛋白质科学研究（上海）设施（以下简称“蛋白质设施”）的蛋白质科学研究机构，也是生化与细胞所学科布局的三大支撑点之一。中心目前处于筹建阶段，办公地点位于生化与细胞所岳阳路园区，筹建期主要任务是聚集培养科研、技术、管理人才，支撑蛋白质设施建设。2012 年底之前，蛋白质中心将逐步进驻位于浦东张江高科技园区的蛋白质设施。2013 年底设施正式投入运行之后，中心主要任务将包括：1) 运营和管理蛋白质设施，服务设施用户；2) 开展前瞻性的蛋白质科学基础研究和技术开发；3) 积极开展基于原创科研成果的转化型研究。

自 2009 年以来，生化与细胞所全力推进中心各项筹建工作，目前在高端人才引进、技术人才培训、行政管理队伍建设等方面已取得了长足进展。

## 中心领导



雷　鸣 研究员

中心主任

生化与细胞所副所长

回国前：密西根大学副教授(终身)，HHMI青年科学家

周界文 研究员

中心副主任

回国前：哈佛大学副教授(终身)

张荣光 研究员

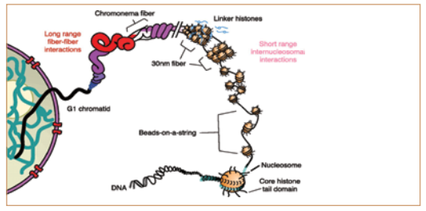
中心副主任

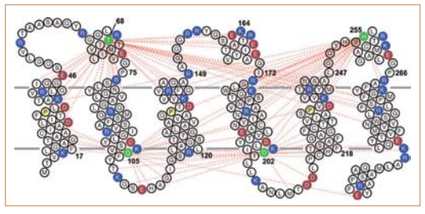
回国前：阿贡国家实验室研究员

## 组织结构

染色体组织构架

染色体相关生物大分子的结构、功能与调控



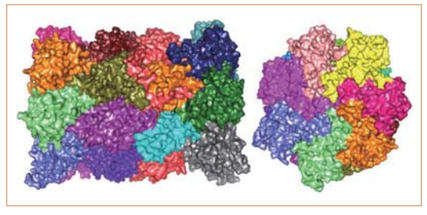



跨膜生物学过程

跨膜物质运输、信号传导及细胞间通讯

生物大分子机器

重要生物大分子机器的结构、功能及调控





国家蛋白质科学综合研究中心(上海)

## 国家蛋白质科学研究(上海)设施

国家蛋白质科学研究（上海）设施（以下简称“蛋白质设施”）是我国首个国家级、综合性蛋白质科学研究设施，也是我国生命科学领域首个国家重大科技基础设施项目。项目依托中科院上海生科院，主要由生化与细胞所建设、管理，总投资 7 亿元，建设期 3 年，建设地点位于上海市张江高科技园区。项目已于 2010 年 12 月 26 日正式开工，预计于 2013 年底正式投入运行。

建成后的蛋白质设施总建筑面积约为 33,550 平方米，在物理位置上分为两个部分：一、具备规模化蛋白质制备、核磁分析、电镜分析、质谱分析、复核激光显微成像、分子影像（部分）、数据库与计算机分析等技术系统的生化与细胞所 / 蛋白质设施海科园区；二、位于上海同步辐射光源内的，具备蛋白质晶体结构分析、蛋白质动态分析和分子成像（部分）等技术系统的光束线站。


## 生化与细胞所全力投入蛋白质设施建设

**工程建设经理部**

| | | | |
|---|---|---|---|
| 吴家睿 | 首席科学家，副总经理 | 雷　鸣 | 总工艺师 |
| 李　林 | 副总经理 | 张荣光 | 副总工程师 |
| 景乃禾 | 副总经理，总工程师 | 周界文 | 副总工艺师 |

**线站部**

| | |
|---|---|
| 张荣光 | 副主任 |

**第一系统: 规模化蛋白质制备**

| | |
|---|---|
| 雷　鸣 | 主任设计师 |
| 周兆才，黄　昊 | 副主任设计师 |

**第三系统: 蛋白质核磁分析**

| | |
|---|---|
| 胡红雨 | 主任设计师 |
| 许琛琦 | 副主任设计师 |

**第四系统: 集成化电镜分析**

| | |
|---|---|
| 景乃禾 | 主任设计师 |
| 丛　尧，何勇宁 | 副主任设计师 |

**第六系统: 蛋白质修饰与相互作用分析**

| | |
|---|---|
| 曾　嵘 | 主任设计师 |

**第七系统: 复合激光显微镜**

| | |
|---|---|
| 朱学良 | 主任设计师 |
| 边　玮 | 副主任设计师 |

**第八系统: 分子影像**

| | |
|---|---|
| 朱学良 | 主任设计师 |
| 胡荣贵 | 副主任设计师 |

**动物设施**

| | |
|---|---|
| 刘小龙 | 主任设计师 |
| 陈浩杰 | 副主任设计师 |

# 国际交流合作

国际专家顾问委员会

年轻PI学术顾问委员会

国际学术会议

国际及地区合作

其他国际交流合作活动

第二十一届国际生物化学与分子生物学联盟学术大会暨第十二届亚洲大洋洲生物化学家与分子生物学家学术大会
(2009年8月2日 - 7日)

# 国际专家顾问委员会

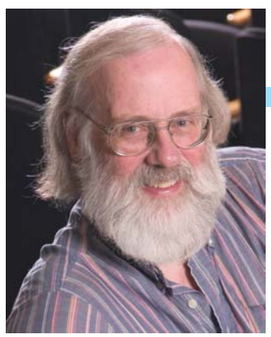
2010 年，生化与细胞所聘请 7 位国际顶尖学者组成国际专家顾问委员会。从 2012 年开始，委员会将定期召开会议，委员们将利用他们丰富的学术和管理经验，为营造学者型研究环境、创建国际一流研究所出谋划策。

## Sidney Altman 博士

耶鲁大学教授
美国国家科学院院士
1989 年诺贝尔化学奖得主
RNA 领域的先驱者

## Melanie Cobb 博士

德州大学西南医学中心教授
美国国家科学院院士
细胞信号转导领域的先驱者

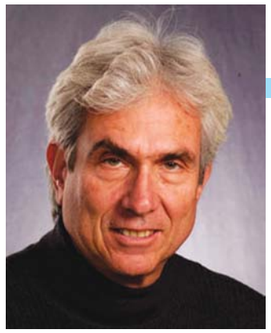


## Tony Hunter 博士

萨克研究所教授
美国国家科学院院士
英国皇家学会会员
蛋白质重大修饰的发现者



国际专家顾问委员会



## Michael Karin 博士

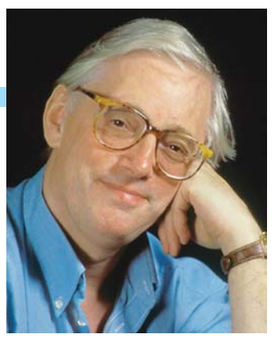
加州大学圣地亚哥分校教授
美国国家科学院院士
细胞信号转导与基因调控领域的先驱者

## Roel Nusse 博士

斯坦福大学教授
美国国家科学院院士
细胞信号转导与干细胞领域的先驱者

## Janet Rossant 博士

多伦多大学教授
加拿大、英国皇家学会会员
美国国家科学院外籍院士
发育与干细胞领域的先驱者



## John Walker 博士

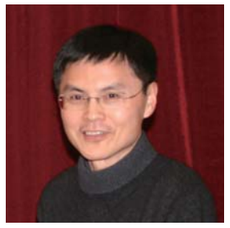
剑桥大学教授
英国皇家学会会员
美国国家科学院外籍院士
1997 年诺贝尔化学奖得主
结构生物学领域的权威

# 年轻PI学术顾问委员会

在“信号转导研究”创新团队国际合作伙伴计划项目 (2005-2009) 的成功经验基础上，生化与细胞所于 2009 年在国内率先建立年轻 PI 学术顾问委员会。目前委员会由 18 名知名华裔学者组成，他们为年轻 PI 提供学术指导，并促进年轻 PI 与国际学术界的交流。


杜　巍 博士
芝加哥大学教授

傅向东 博士
加州大学圣地亚哥分校教授

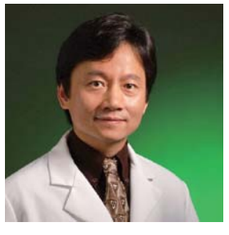



顾　华 博士
麦基尔大学教授

管俊林 博士
密西根大学教授


管坤良 博士
加州大学圣地亚哥分校教授

韩家淮 博士
厦门大学教授

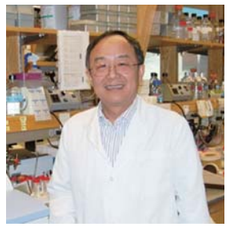



林海凡 博士
耶鲁大学教授

刘正刚 博士
美国国立癌症研究所高级研究员



年轻PI学术顾问委员会

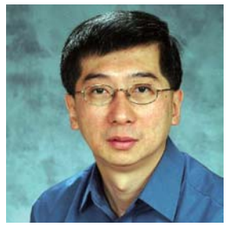



孙少聪 博士
德州大学MD Anderson癌症中心教授

王小凡 博士
杜克大学教授


吴殿青 博士
耶鲁大学教授

吴　浩 博士
哈佛大学教授

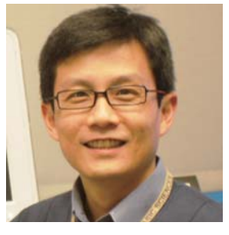



解　亭 博士
堪萨斯大学教授

许志忠 博士
多伦多大学教授


杨英姿 博士
美国国立人类基因组研究所高级研究员

赵　华 博士
贝勒医学院教授

郑诣先 博士
华盛顿卡内基研究院高级研究员

朱　衡 博士
约翰霍普金斯大学教授

# 国际学术会议

从 2009 年到 2011 年，研究所共主办国际学术会议 20 次，参会人数 4,900 多人。这些学术会议极大地促进了国内外科学家的学术交流和合作，同时也展现了研究所的科研实力，提高了研究所的国际学术影响力。

## 第三届信号转导、炎症与癌症上海国际研讨会

**The 3rd Shanghai Symposium: Signaling, Inflammation and Cancer** 2011 年 7 月 25 日 - 28 日

### 主办单位

生化与细胞所

美国国立癌症研究所

### 概况

7 个专题，43 位报告人（包括 27 位国外报告人），报告内容涉及细胞信号转导机理、细胞死亡和自吞噬、信号转导与炎症、信号转导与癌症、炎症与癌症，国内外参会人数达 400 余人

## 第四届纪念曹天钦蛋白质研究国际研讨会

**The 4th CAO Tianqin Memorial Symposium on Protein Research** 2010 年 12 月 5 日 - 8 日


### 主办单位

曹天钦基金会

生化与细胞所

厦门大学生命科学学院

### 概况

9 个专题，43 位报告人（包括 23 位国外报告人），报告内容涉及蛋白质结构与功能、蛋白酶和其他酶蛋白、信号转导、肌肉蛋白和毒素、蛋白质与肿瘤、免疫蛋白与病毒蛋白等，国内外参会人数达 200 余人

## 第二十一届国际生物化学与分子生物学联盟学术大会暨第十二届亚洲大洋洲生物化学家与分子生物学家学术大会

**21st IUBMB and 12th FAOBMB International Congress of Biochemistry and Molecular Biology** 2009 年 8 月 2 日 - 7 日

### 主办单位

国际生物化学与分子生物学联盟 (IUBMB)

亚洲大洋洲生物化学家与分子生物学家联合会 (FAOBMB)

中国生物化学与分子生物学会

中国细胞生物学学会

生化与细胞所

### 概况

36 个专题，254 位报告人（包括 4 位诺贝尔获得者），报告内容涵盖了基因组动态和基因调控、蛋白质结构动态和蛋白质组学、细胞信号转导和网络、以及疾病的分子基础，国内外参会人数达 3,000 余人



# 国际及地区合作

## 亚太国际分子生物学网络组织(A-IMBN)

生化与细胞所是亚太国际分子生物学网络组织 (A-IMBN) 创始成员之一。从 2002 年开始，在 AIMBN 的合作框架下，生化与细胞所与台湾大学生物化学与分子生物学研究所 (IBMB)、日本东京大学医学科学研究所 (IMS)、日本京都大学病毒研究所 (IVR)、韩国首尔大学分子生物学与遗传学研究所 (IMBG)、韩国成均馆大学三星生物医学研究所 (SBRI) 等三国六所共同举办东亚生物医学研讨会，每年轮流在中国大陆、中国台湾、日本、韩国举行，对中、日、韩三国的生物医学交流合作起到了很好的推动促进作用。

## 海峡两岸生物医学研讨会

从 2001 年开始，生化与细胞所与台湾大学生物化学与分子生物学研究所共同举办海峡两岸生物医学研讨会，每年轮流在大陆和台湾举办，至 2011 年已成功举办了 10 届，有力地促进了两岸科学家的相互了解和交流合作。

# 国际及地区合作

## 其他国际及地区合作伙伴

美国国立健康研究院、阿贡国家实验室、芝加哥大学、耶鲁大学、艾默里大学、欧洲分子生物学实验室等著名研究机构的相关实验室已同意为国家蛋白质中心培训技术人员，已有一批技术人员赴美接受培训。目前已有技术人员培训完成回国参与国家蛋白质设施建设。

2007 年，生化与细胞所与加拿大多伦多大学分子遗传学系、Terrence Donnelly 细胞与生物分子研究中心和附属病孩医院签订了在干细胞生物学和功能基因组学领域进行合作的框架协议，至 2011 年已在上海和多伦多成功举办了三次学术研讨会。此外，研究所与美国耶鲁大学细胞生物学系和耶鲁干细胞中心积极谋求建立更紧密的合作关系，将在 2012 年底在上海召开第一次学术研讨会。

此外，生化与细胞所与英国医学研究理事会 (MRC)、法国国家科学研究院 (CNRS)、法国国家健康和医学研究院 (INSERM)、德国马普学会 (MPG)、俄国莫斯科国立大学、香港大学都保持着良好的交流合作关系。



# 其他国际交流合作活动

## 王应睐讲座

2011 年，生化与细胞所设立了年度系列“王应睐讲座”以缅怀王应睐院士（研究所创始人之一），推动高端国际学术交流。研究所建立了严格的评选程序，在全球范围内选择并邀请那些在各自领域被公认为领导者 / 开拓者的著名生物学家来为本所及来自上海其他研究机构的科研人员作报告，并进行学术交流。

Dr. Don Cleveland
(2012 年 4 月 23 日 )

Dr. Dieter Söll
(2011 年 12 月 13 日 )

Dr. Gary Felsenfeld
(2011 年 9 月 13 日 )

Dr. Elaine Fuchs
(2011 年 10 月 28 日 )

## 国际期刊编委

| | | |
|---|---|---|
| 景乃禾，李 林，王恩多，吴家睿 | | |
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| 宋建国 | 吴家睿 | 丁小燕，景乃禾 |
| 景乃禾，吴家睿 | | |
| 陈正军 | 景乃禾 | |
| 景乃禾 | | 丁建平，周界文 |
| 景乃禾 | | 王 纲 |
| 胡红雨 | | |

## 来访及出访概况

2009-2011 年，1,065 人次来研究所进行学术交流，353 人次出国进行学术交流。

2010 年 4 月 9 日，1962 年诺贝尔生理学或医学奖得主 Dr. James Watson 来所访问交流

2011 年 10 月 26 日，2009 年诺贝尔化学奖得主 Dr. Thomas A. Steitz 及 Dr. Venkatraman Ramakrishnan 来所访问交流

# 研究生教育

研究生教育

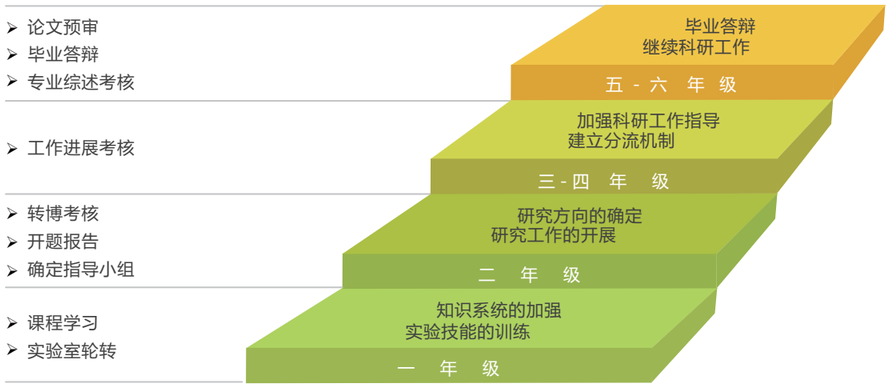
研究生风采

## 研究生教育

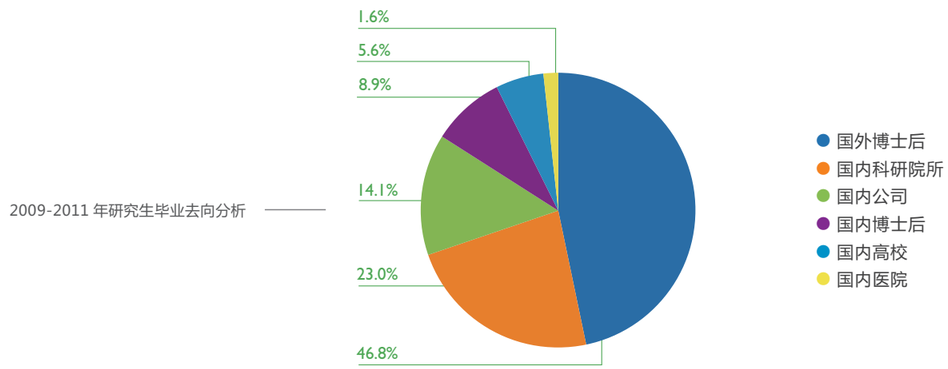
生化与细胞所设有生物化学与分子生物学，细胞生物学，发育生物学三个招生专业，2012 年 7 月底时，在读研究生共总数为 428 人，其中博士生 293 人，硕士生 135 人。

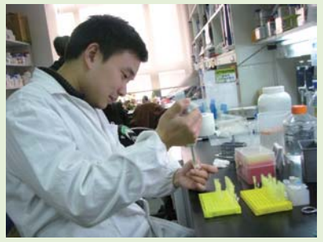
## 研究生培养体系

- 创建与国际接轨的研究生培养体系，提高培养水平：实验室轮转、导师指导小组、精品课程
- 强化过程管理，保障培养质量：转博考核、年度进展考核、分流淘汰机制
- 构建学术交流平台，开阔学生视野：国内外学术会议、研究所、国家重点实验室学术年会、学术报告、研究生学术沙龙、第一作者讲坛




## 研究生毕业去向





研究生在做实验

研究生参加第六届思齐讲坛
(2011 年 6 月 17 日 )

研究生与参加夏令营活动的本科生进行交流
(2011 年 7 月 18 日 - 22 日 )

两位生化与细胞所研究生代表，岳锐和葛亮 ( 第二排右三及右四 ) ，参加 2010 年林岛诺贝尔奖获得者大会
(2010 年 6 月 27 日至 7 月 2 日 )

研究生廖婧 ( 左三 ) 参加诺华瑞士总部 BioCamp 活动
(2010 年 9 月 6 日 )

研究所中秋游园会
(2011 年 9 月 14 日 )

研究所篮球队勇夺上海分院篮球赛冠军
(2011 年 6 月 12 日 )





## 研究生奖励和荣誉(2009-2012)

| 奖励荣誉名称 | 获奖学生(所属导师) |
|---|---|
| 吴瑞奖学金 | 2012 黄鹏羽 (惠利健)，杨　辉(李劲松)，顾天鹏(徐国良)<br>2010 岳　锐 (裴　钢)<br>2009 马　丽 (朱学良) |
| 全国优秀博士学位论文奖 | 2011 王晓明(刘小龙)<br>2009 施裕丰(裴　钢) |
| 中科院优秀博士学位论文奖 | 2011 马　丽(朱学良)<br>2010 栾　冰(裴　钢)，王晓明(刘小龙)，曹　剑(宋保亮)<br>2009 施木德(孙　兵) |
| 中科院院长特等奖 | 2011 黄鹏羽(惠利健)，潘有东(陈剑峰)<br>2010 岳　锐(裴　钢)<br>2009 栾　冰(裴　钢) |
| 中科院院长优秀奖 | 2011 李振斐(李　林)，唐静洁(宋保亮)<br>2010 胡佳磊(徐国良)，廖　婧(肖　磊)，刘　畅(裴　钢)<br>2009 项　阳(陈德桂)，孟飞龙(周金秋)，马　丽(朱学良) |
| 地奥奖学金一等奖 | 2011 周旻昀(丁建平)，高益军(季红斌)<br>2010 周旻昀(丁建平)，石贺欣(王　琛)<br>2009 张振宁(鲍　岚)，周小龙(王恩多) |
| 朱李月华优秀博士生奖学金 | 2011 陈涛涛(裴　钢)，张　渊(孙　兵)<br>2010 伍一博(曾　嵘)<br>2009 印　敏(周嘉伟) |
| BHP Billiton奖学金 | 2010 岳　锐(裴　钢)<br>2009 葛　亮(宋保亮) |
| 辉瑞奖学金特别奖 | 2011 孙兵法(丁建平)，张燕燕(赵　允)<br>2010 周　波(周金秋)，董咸池(丁建平)，朴香花(吴立刚) |

生化与细胞所岳阳路园区盛开的樱花