科学需要人的全部生命去探索

王应睐

"Science calls for our lifelong dedication."

*Prof. Yinglai Wang*

Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences
320 Yueyang Road, Xuhui District, Shanghai, 200031 China
+86-(0)21-54920000 (T)
+86-(0)21-54921011 (F)
sibcb@sibs.ac.cn
www.sibcb.ac.cn

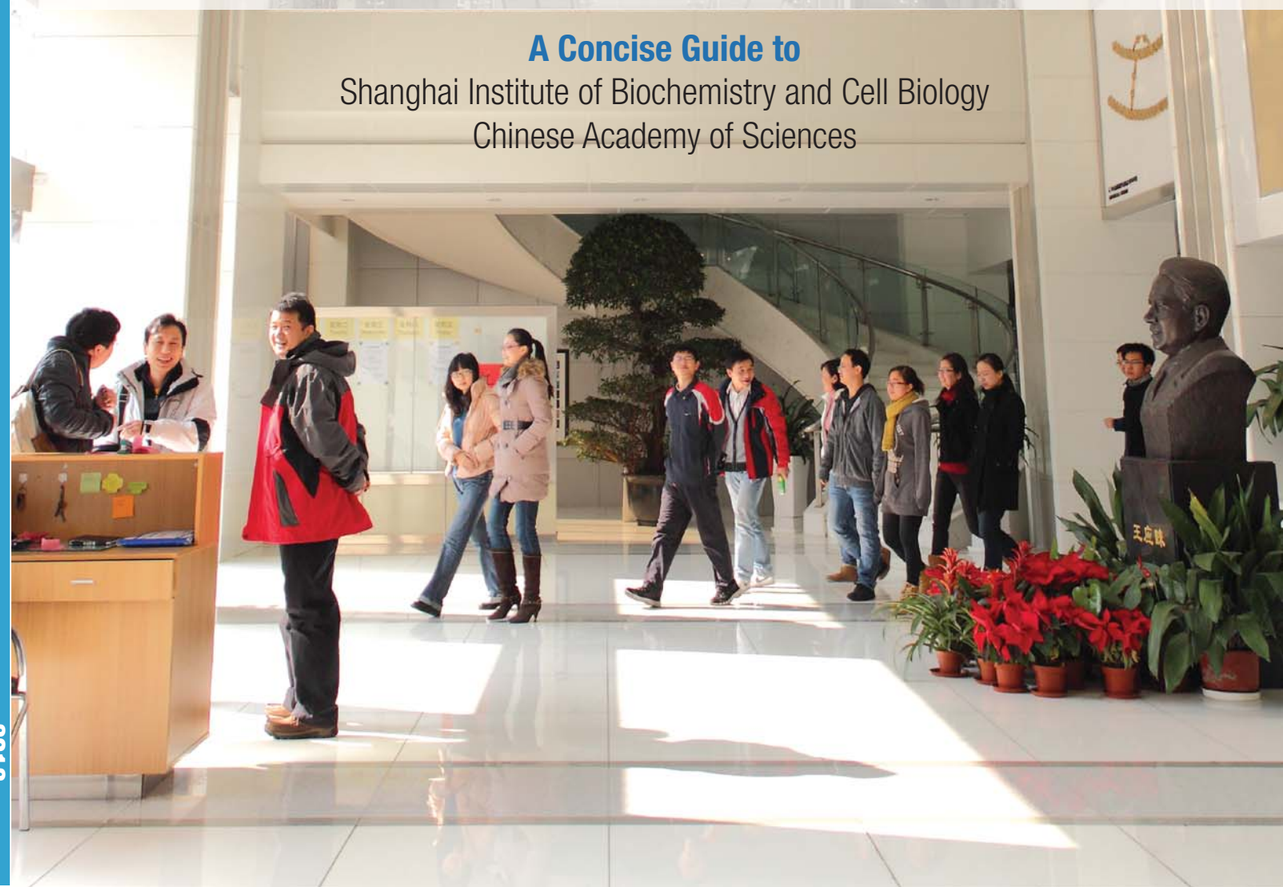
SIBCB

www.sibcb.ac.cn

# SIBCB

## A Concise Guide to

Shanghai Institute of Biochemistry and Cell Biology
Chinese Academy of Sciences



2012

# SIBCB



Welcome to SIBCB, China's leading biomedical research institute located in central Shanghai.

SIBCB Yueyang Campus

# Introduction



The statue of Prof. Yinglai Wang (left), founding director of SIB, in the lobby of Building B; and the statute of Prof. Xi Zhu (right), the second director of IEB, in front of Building C

## From the Director

Anning Lin, Ph.D.
Professor and Director

The history of Shanghai Institute of Biochemistry and Cell Biology (SIBCB), Chinese Academy of Sciences (CAS) can be traced back to 1950's, when a small group of talented biochemists and cell biologists, headed by Professor Yinglai Wang and Professor Shizhang Bei, founded Shanghai Institute of Biochemistry (SIB), CAS, and Shanghai Institute of Cell Biology (SICB), CAS, respectively, in Shanghai. Nearly 50 years after their inception, SIB and SICB merged to become SIBCB at the beginning of the new millennium. Building on SIB/SICB's scientific legacy such as the synthesis of bovine insulin (1965) and the synthesis of yeast $tRNA^{Ala}$ (1981), SIBCB scientists are conducting cutting-edge research not only to advance the frontiers of modern biology such as gene regulation/RNA/epigenetics, protein science, cell signaling and cell/stem cell biology, but also to tackle major medical problems such as metabolic diseases, neurodegenerative diseases and cancer. Not satisfied with the status quo of being a leading biomedical research institute in China, SIBCB is making great efforts to boost its research teams, extramural funding, core facilities and graduate program, which collectively constitute an inspiring and supportive scholarly research environment to fulfill the Institute's ambition of becoming an internationally renowned institute.

Currently, SIBCB has 66 research laboratories led by talented principal investigators and supported by 850-strong research staff, postdoctoral fellows and Ph.D. students. Pursuing academic excellence is in the DNA of SIBCB faculty, staff and students, demonstrated by a long track record of seminal findings. For instance, over the past three years, 6 major findings made by SIBCB faculty have been published in high-profile journals such as *Cell*, *Nature* and *Science*, and 59 major findings ranging from gene regulation to molecular medicine have appeared on high-profile journals including *Cell Stem Cell*, *Molecular Cell*, *Developmental Cell*, *Cell Metabolism*, *Nature Immunology*, *Nature Cell Biology*, *Nature Structural & Molecular Biology*, *Neuron*, *PNAS*, *EMBO Journal*, *Gastroenterology*, *Hepatology* and *Blood*.

Research at SIBCB is organized around three major "clusters", namely the State Key Laboratory of Molecular Biology (SLMB), the State Key Laboratory of Cell Biology (SKLCB) and the National Center for Comprehensive Protein Science Shanghai (NCPS Shanghai). State key laboratories, reminiscent of MRC centers in British universities, are in fact "national centers of excellence" that receive financial support and administrative supervision from the Chinese central government. NCPS Shanghai is an exciting new development of the Institute since 2009: it is the in-house research team of the National Facility for Protein Science in Shanghai (NFPS Shanghai), which is a ¥ 700 million, 33,550 $m^2$, state-of-the-art research facility expected to put into service at the end of 2013.

Biology is undoubtedly one of the most important disciplines in the 21$^{st}$ century. Research in biochemistry, molecular biology and cell biology not only uncovers the secrets of life, but also provides insights and therapeutic targets for modern medicine. As a leading biomedical research institute in China and hopefully in the world in the near future, SIBCB will continuously make important contributions to the advancement of biology and improvement of human health in years to come.

# History

The history of Shanghai Institute of Biochemistry (SIB), CAS can be traced back to the Biochemistry Unit of the Institute of Physiology and Biochemistry, CAS, which was established in 1950. From 1950 to 2000, SIB scientists published nearly 4,000 research articles, received 178 national, provincial and municipal awards (including 4 national 1st grade awards and 9 national 2nd grade awards), and trained 255 master students and 171 doctoral students.

The history of Shanghai Institute of Cell Biology (SICB), CAS can be traced back to the Institute of Experimental Biology (IEB), CAS, which was established in 1950. From 1950 to 2000, SICB scientists published nearly 1,600 research articles, received 92 national, provincial and municipal awards (including 1 national 1st grade award and 2 national 2nd grade awards), and trained 112 master students and 107 doctoral students.

In 2000, SIB and SICB merged to become Shanghai Institute of Biochemistry and Cell Biology (SIBCB), CAS.


**1958** The main entrance of the Yueyang campus, with the name plaque of IEB on the left, and that of SIB on the right (c.a. 1958)





## SIB

**1959**


The group photo of the Institute's personnel on the 10th National Day (September 30th)

Prof. Jingyi Niu (center) and his colleagues discussing new approaches of polypeptide synthesis

**1986**

The appraisal meeting of the State Key Laboratory of Molecular Biology organized by State Planning Commission and Chinese Academy of Sciences (December 17th)

**1997**


The celebration meeting for SIB's 40th anniversary and Prof. Yinglai Wang's 90th birthday (November 13th )

**1999**

The SIB Research Building

## SICB

**1961**

Prof. Xi Zhu (2nd from left) analyzing and explaining the experimental records of toad artificial parthenogenesis

**1981**


The group photo of the first batch of master students admitted after the Cultural Revolution (Grade 1978) together with their supervisors

**1985**

The opening ceremony of the Max Planck Guest Laboratory (April 4th)

**1991**

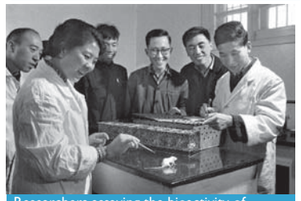
German guests, accompanied by Prof. Xiaohui Zhuang, Prof. Yahui Wang and Prof. Lihe Guo, visited the Max Planck Guest Laboratory

**1999**

The SICB Research Building

# History

Primary structure of bovine insulin
(Sequenced by Frederick Sanger in 1951)



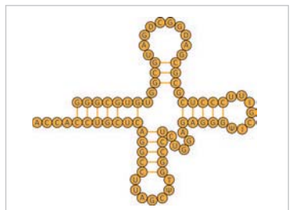
Researchers assaying the bioactivity of synthesized bovine insulin

Vice premier Rongzhen Nie with the partici-pants of the insulin synthesis project final assessment conference(the Great Hall of the People, December 14th, 1978)

National Natural Science Award
(1st grade, 1982)

## Total Synthesis of Crystalline Bovine Insulin

- 1958 Proposition of the Total Synthesis of Bovine Insulin Project
- 1959 Successful separation and recombination of natural insulin A/B chain
- 1960 Launch of nationwide collaboration for insulin synthesis/ Successful synthesis of A chain and B chain/ The Grand Campaign of Insulin Synthesis
- 1963 Re-start of nationwide collaboration including SIB-CAS, PKU Dept. of Chemistry and SIOC-CAS
- 1964 Successful combination of the synthesized A and B chain (weak bioactivity detected)
- 1965 Successful synthesis of crystalline bovine insulin, the world's first synthesized protein that has the same chemical structure as its natural counterpart and exhibits full bioactivity
- 1966 *Science* magazine published "Total Synthesis of Insulin in Red China" to report the achievement of Chinese scientists
- 1982 Total Synthesis of Bovine Insulin received the National Natural Science Award (1st grade)



Primary structure of yeast $tRNA^{Ala}$
(Sequenced by Robert Holley in 1964)

Prof. Debao Wang (center) with some members of the Collaboration Group

## Total Synthesis of Yeast Alanine Transfer Ribonucleic Acid ($tRNA^{Ala}$)

- Proposition of the Total Synthesis of Yeast $tRNA^{Ala}$ Project 1967
- Lanuch of the $tRNA^{Ala}$ Synthesis Project, Shanghai participating institutions including SIB-CAS (leading), SICB-CAS and SIOC-CAS 1968
- Successful synthesis of an 8-nucleoside 7- phosphate fragment 1974
- Establishment of the $tRNA^{Ala}$ Syntheis Project Collaboration Group within CAS 1977
- Establishment of three Campaign Groups (Large Fragment Synthesis, Final Assembly and Bioactivity Detection) 1978
- Successful synthesis of yeast $tRNA^{Ala}$, the world's first synthesized ribonucleic acid that has the same chemical structure as its natural counterpart and exhibits full bioactivity 1981
- *Nature* magazine published "Nucleic Acid Synthesis, Pinyin tRNA" to report the achievement of Chinese scientists 1983
- Total Synthesis of Yeast $tRNA^{Ala}$ received the National Natural Science Award (1st grade) 1987

Participants of the CAS Yeast $tRNA^{Ala}$ Synthesis Symposium
(Beijing Science Hall, Jan 18th, 1982)

National Natural Science Award
(1st grade, 1987)



# Academic Organization

## Three Clusters

See p55-p60 for details

### State Key Laboratory of Molecular Biology

Prof. Lin Li
Director

### State Key Laboratory of Cell Biology

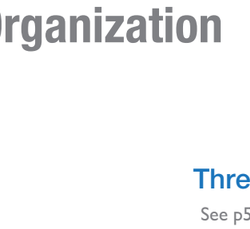
Prof. Xueliang Zhu
Director

### National Center for Comprehensive Protein Science Shanghai

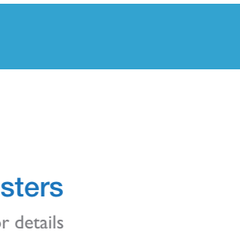
Prof. Ming Lei
Director

## Five Areas

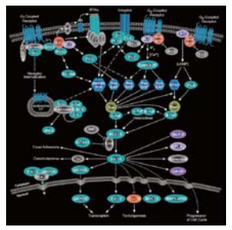
see p15-p50 for research highlights



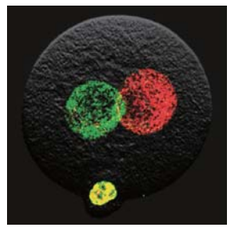
Gene Regulation, RNA and Epigenetics



Protein Science



Cellular Signal Transduction



Cell and Stem Cell Biology

Cancer and Other Diseases

# Strategic Plan (2011-2015)

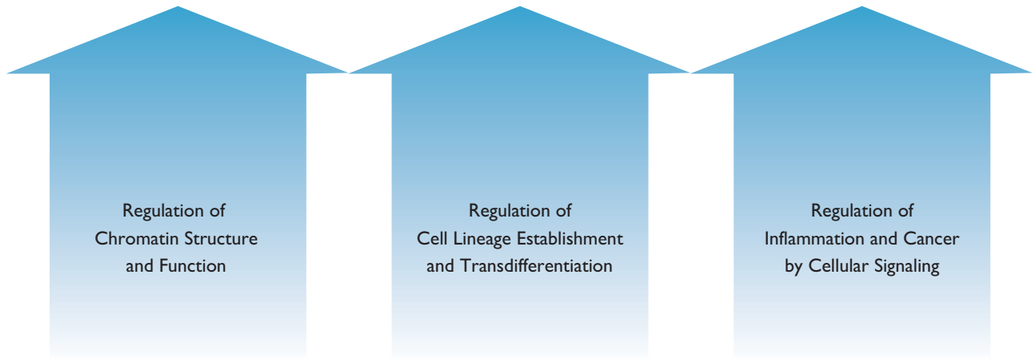
## Mission

The mission of SIBCB is to conduct innovative research in the frontiers of modern biology including biochemistry, molecular biology and cell biology, to advance the mechanistic understanding of life, and to provide insights and therapeutic targets for modern medicine.

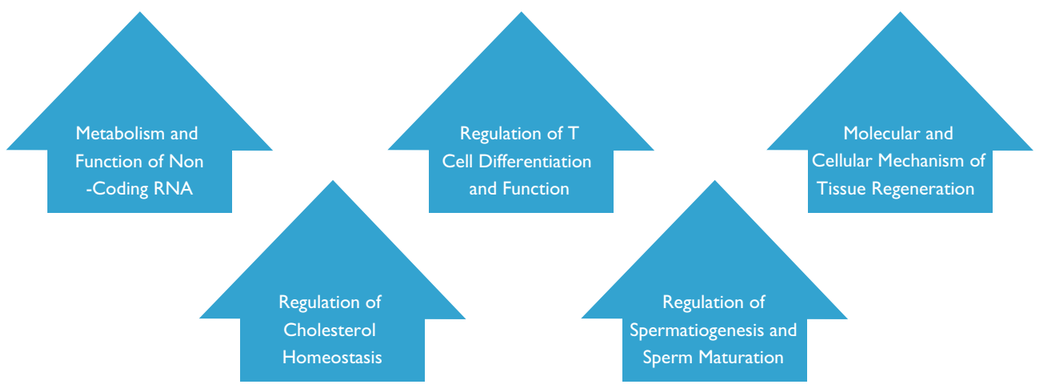
## Development Goals

- Build a scholarly research environment that encourages innovative research, supports productive collaboration, and promotes discovery.
- Become an internationally renowned institute with leading scientists who make significant findings in a continuous and systematic manner, and are regarded as leaders in their fields by the international academic community.

## Three Major Research Initiatives



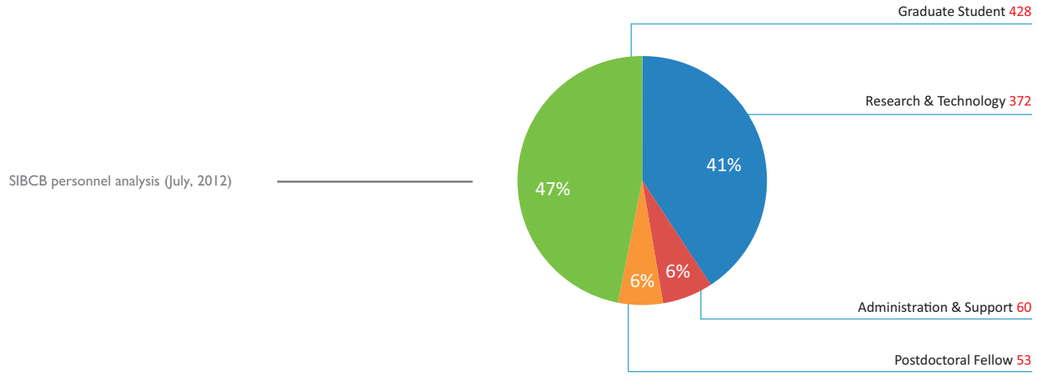

## Five Additional Research Directions



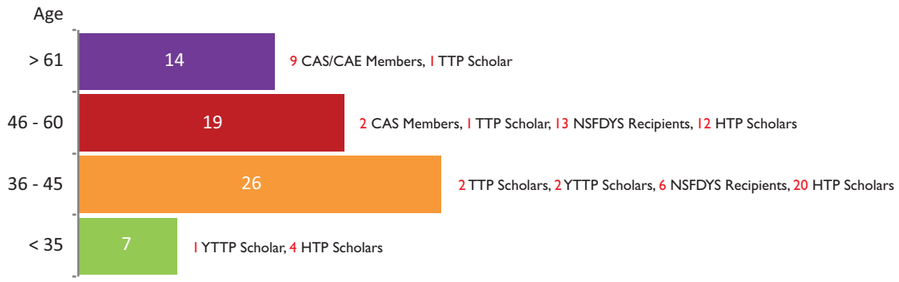



# Principal Investigators

At the end of July, 2012, SIBCB has 913 personnel including faculty, staff and students. At the core of the Institute's research team are 66 principal investigators (PIs), including 10 Chinese Academy of Sciences Members (CAS Members), 1 Chinese Academy of Engineering Member (CAE Member), 4 Thousand Talents Program (TTP) scholars, 3 Young Thousand Talents Program (YTTP) scholars, 19 recipients of the National Science Fund for Distinguished Young Scholars (NSFDYS) and 36 Hundred Talents Program (HTP) scholars.



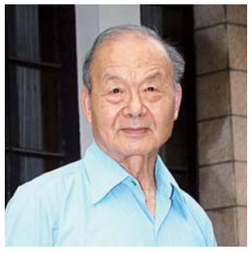

SIBCB personnel analysis (July, 2012)




Age distribution of SIBCB PIs (July, 2012)

## PI Awards and Honors (2009-2012)

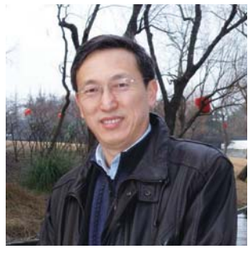
| PI | Award/Honor | Year |
|---|---|---|
| Baoliang Song | Jiageng Chen Youth Science Award | 2012 |
| Gang Pei | Jiazhen Tan Life Science Achievement Award | 2011 |
| Lijian Hui | Chinese Youth Science and Technology Award | 2011 |
| Jinqiu Zhou | A-IMBN Arthur Kornberg Memorial Award | 2011 |
| Xiaolong Liu | A-IMBN Research Young Investigators Award | 2011 |
| Gang Pei | Jiageng Chen Science Award | 2010 |
| Naihe Jing | Shanghai Leading Talents | 2010 |
| Xiaolong Liu | Chinese Youth Science and Technology Award | 2009 |
| Xueliang Zhu | Shanghai Peony Award for Natural Sciences | 2009 |



**Prof. Xinyuan Liu**
CAS Member, Elected in 1991
Biotherapy of Cancer

**Prof. Yueting Gong**
CAS Member, Elected in 1993
Structure and Function of Bioactive Peptides and Proteins

**Prof. Zaiping Li**
CAE Member, Elected in 1995
HBV/Liver Cancer Related Genes: Identification and Function



**Prof. Guofan Hong**
CAS Member , Elected in 1997
Function of Small RNA in Symbiotic Nitrogen Fixing System

**Prof. Gang Pei**
CAS Member, Elected in 1999
Cellular Signal Transduction

**Prof. Zhengwu Qi**
CAS Member, Elected in 1999
Structure and Function of Bioactive Polypeptides and Enzymes

**Prof. Youshang Zhang**
CAS Member , Elected in 2001
Protein Structure and Function

**Prof. Yonglian Zhang**
CAS Member, Elected in 2001
Molecular Basis of Sperm Maturation in Epididymis

**Prof. Qishui Lin**
CAS Member, Elected in 2003
Structure and Function of Biomembrane

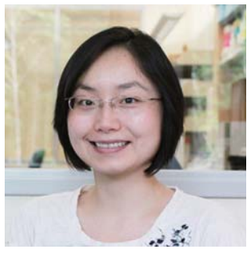
**Prof. Enduo Wang**
CAS Member, Elected in 2005
Quality Control of Protein Biosynthesis

**Prof. Lin Li**
CAS Member, Elected in 2011
Molecular Mechanism and Function of Cellular Signal Transduction and Regulation

**Prof. Lan Bao**
Neuronal Protein Transport

**Prof. Degui Chen**
Epigenetics, Stem Cell and Cancer

**Prof. Jianfeng Chen**
Functional Regulation of Cell Adhesion Molecules in Inflammation and Cancer

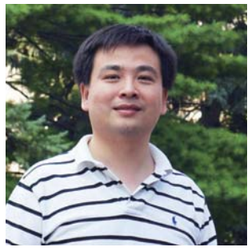


**Prof. Jiangye Chen**
Gene Expression Regulation of Morphogenesis

**Prof. Lingling Chen**
Long Non-Coding RNA and Stem Cell

**Prof. Zhengjun Chen**
Phosphoprotein Signaling Network and Tumorigenesis

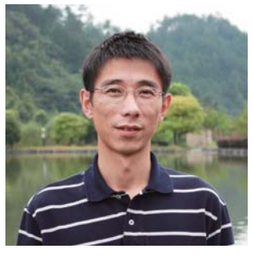




**Prof. Yong Chen**
Structural Biology of Epigenetic Regulation

**Prof. Hong Cheng**
Regulation and Function of Gene Expression

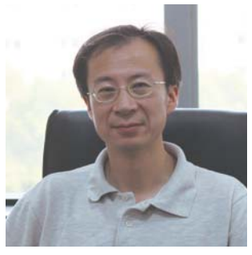
**Prof. Yao Cong**
Structural Biology of Chaperone-Assisted Protein Folding and Disaggregation

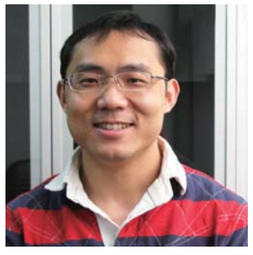


**Prof. Jianping Ding**
Structural Biology of Eukaryotic Gene Expression Regulation

**Prof. Daming Gao**
Cancer Signaling and Metabolism

**Prof. Gaoxiang Ge**
Microenvironmental Regulation of Tumorigenesis and Metastasis





**Prof. Yongning He**
Structural Biology of Cell Surface Receptors and Cell-Cell Interactions

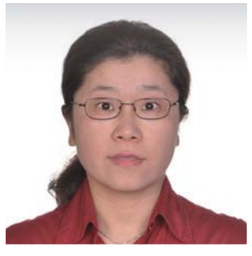
**Prof. Fajian Hou**
Molecular Mechanism of Signal Transduction in Innate Immunity

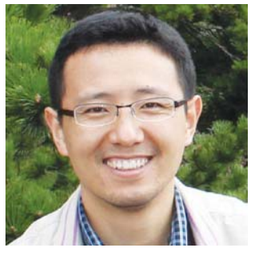
**Prof. Hongyu Hu**
Protein Misfoliding and Degradation

**Prof. Ping Hu**
Adult Stem Cell Fate Determination

**Prof. Ronggui Hu**
Regulated Proteolysis & Molecular Recognition

**Prof. Ying Huang**
Structural Biology of Gene Transcription Regulation

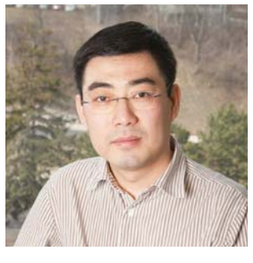




**Prof. Jingyi Hui**
Regulation of RNA Processing

**Prof. Lijian Hui**
Molecular Pathology of Liver Diseases & Regenerative Medicine

**Prof. Hongbin Ji**
Molecular Mechanism of Lung Carcinogenesis



**Prof. Hai Jiang**
Personalized Cancer Medicine & Screening and Development of Novel Anticancer Drugs

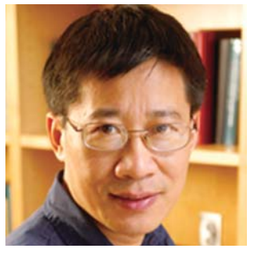
**Prof. Naihe Jing**
Stem Cell & Neural Development

**Prof. Ming Lei**
Structural Biology of Chromatin

Prof. Boliang Li
Expression and Function of Genes Involved in Cholesterol Homeostasis

Prof. Jinsong Li
Somatic Reprogramming & Induced Pluripotent Stem Cell

Prof. Yiping Li
Germ Cells & Embryonic Development



Prof. Kan Liao
Regulation of Cell Proliferation and Differentiation

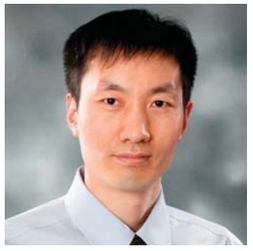
Prof. Lujian Liao
Functional Proteomics & Signaling in Neurodegenerative Diseases

Prof. Anning Lin
Signal Transduction and Gene Regulation

Prof. Dinggan Liu
Function and Regulation of Tumor-Suppressive Nucleic Acid Element

Prof. Mofang Liu
Functions and Mechanisms of Non-Coding RNAs in Cancer and Spermatogenesis

Prof. Xiaolong Liu
T Cell Development and Function



Prof. Kangcheng Ruan
Spectroscopical Study on Structure-Function and Interaction of Biomacromolecules

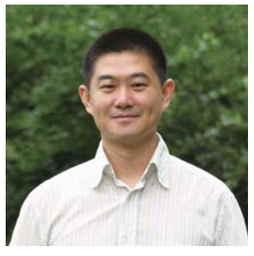
Prof. Baoliang Song
Key Proteins of Cholesterol Metabolism and Their Functional Regulation

Prof. Jianguo Song
Mechanisms of Cell Differentiation and Apoptosis and their Roles in Cancer Progression

Prof. Chen Wang
Molecular Regulation of Host Innate Immunity

Prof. Gang Wang
Regulation of Eukaryotic Gene Expression & Cancer and Stem Cell Biology

Prof. Hongyan Wang
Molecular Mechanism of Lymphocyte Activation and Adhesion



Prof. Jiarui Wu
Protein Regulatory Networks of Cellular Activities & Systems Biology of Complex Diseases

Prof. Ligang Wu
Mechanisms of Gene Regulation by Small Non-Coding RNAs

Prof. Chenqi Xu
Lymphocyte Signal Transduction



Prof. Guoliang Xu
Epigenetic Regulation and its Role in Cancer and Other Diseases

Prof. Rong Zeng
Proteomics and Protein Dynamic Behaviors

Prof. Yi Zeng
Adult Stem Cell Regulation & Stem Cell-Niche Interaction

Prof. Lei Zhang
Regulation of Tissue Differentiation and Growth during Development

Prof. Xuejun Zhang
Apoptosis: Molecular Mechanism and its Role in Diseases

Prof. Mujun Zhao
Function and Regulation of Tumor Related Genes

Prof. Yun Zhao
Molecular Mechanism of Cellular Signaling Abnormality and Pathogenesis

Prof. Jiewen Zhou (James Chou)
Molecular Mechanism of Transmembrane Transport

Prof. Jinqiu Zhou
Chromatin and Cellular Aging

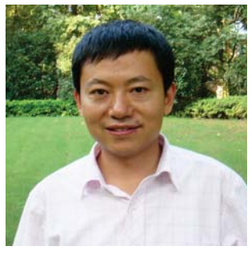
Prof. Zhaocai Zhou
Structural and Molecular Mechanism of GCK Signaling

Prof. Xueliang Zhu
Cell Cycle and Cell Motility

Prof. Weiguo Zou
Molecular Basis of Skeletal Development and Aging

## Adjunct PI

Prof. Rongguang Zhang
Protein Structure and Function & Methodology of Structural Biology



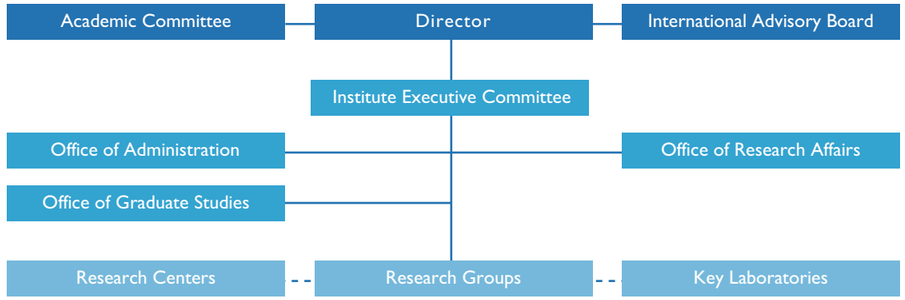
## Guest PI

Prof. Dangsheng Li
Deputy Editor in Chief, *Cell Research*

Prof. Bing Sun
Dendritic Cell Maturation & TH Cell Differentiation

# Administration

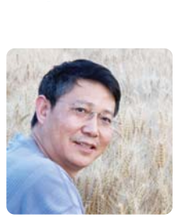
## Administrative Organization



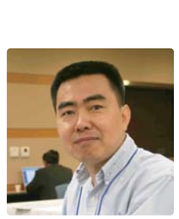

## Principal Officers

Anning Lin
Director

Naihe Jing
Executive Director



Xueliang Zhu
Deputy Director



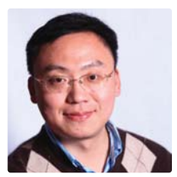
Jinqiu Zhou
Deputy Director

Ming Lei
Deputy Director

Jinhua Guo
Deputy CCP Secretary

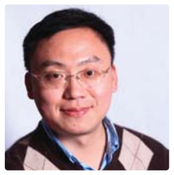
Zhengjun Chen
Assistant Director

Gang Wang
Assistant Director

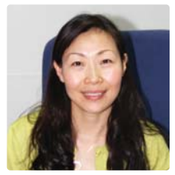


Ge Jiang
Assistant Director

## Administrative Officers



Ge Jiang
Director, Office of Research Affairs



Jinfang Song
Director, Office of Administration

Xianghui Bo
Executive Director, Office of Graduate Studies



Budding laurel trees around Building A

# Research & Development



**A microRNA regulating ciliogenesis.**
In cultured HEK293T cells, overexpression of miR-129-3p induces formation of primary cilia in proliferating interphase cells.

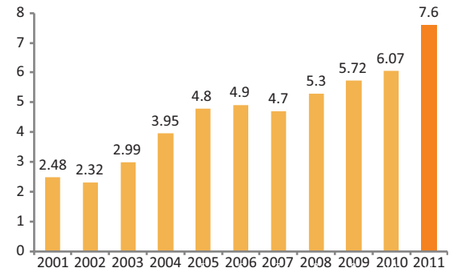
## Overview

### Publications

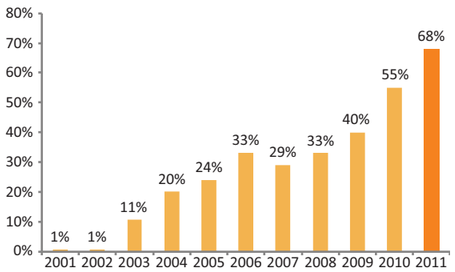
From 2009 to July 2012, SIBCB researchers published 388 research articles including:

6 research articles in top journals including *Cell* (2), *Nature* (3) and *Science* (1)

59 research articles in high profile journals including *Cell Stem Cell* (2), *Developmental Cell* (3), *Molecular Cell* (1), *Cell Metabolism* (2), *Nature Immunology* (2), *Nature Cell Biology* (2), *Nature Structural & Molecular Biology* (1), *Neuron* (1), *Proceedings of the National Academy of Sciences USA* (10), *EMBO Journal* (3), *PLoS Biology* (1), *PLoS Genetics* (2), *Gastroenterology* (2), *Hepatology* (4) and *Blood* (2)




2001-2011 SIBCB publications: average impact factor (IF)

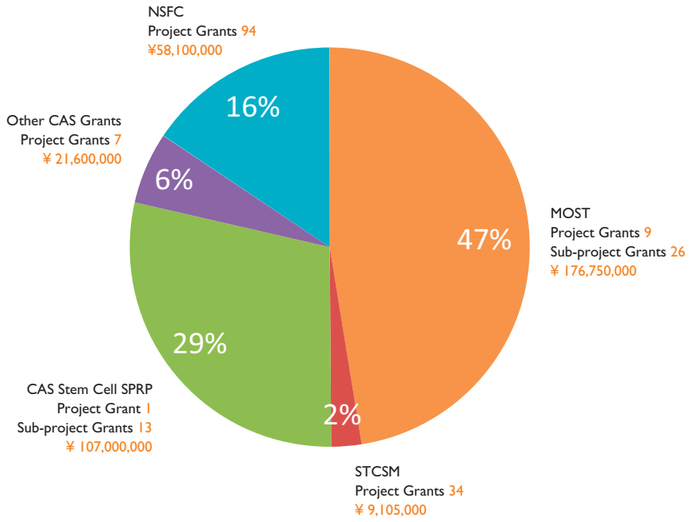



2001-2011 SIBCB publications: percentage of IF≥ *JBC* publications

### Research Awards and Honors (2001-2011)

| Year | Scientific Achievement | Awards/Honors |
|---|---|---|
| 2011 | Successfully Converting Mouse Fibroblasts to Functional Hepatocyte-like Cells | Top 10 Achievements of Chinese Science |
| | Revealing the Important Role of Tet Dioxygenases in Mammalian Epigenetic Regulation | |
| 2009 | Deficiency of a β-Arrestin-2 Signal Complex Contributes to Insulin Resistance | Top 10 News of Chinese Basic Research |
| 2007 | β-Arrestin-2 is a Key Regulator of $CD4^+$ T Cell Survival and Autoimmunity | |
| 2008 | Molecular Basis of Sperm Maturation in Epididymis | National Natural Science Award ($2^{nd}$ grade) |
| 2007 | Mechanism of Crosstalk between GPCR Signaling and Other Signaling Pathways | |
| 2005 | Structure and Function of Ribosome Inactivating Protein and Ribosomal RNA | |
| 2001 | Aminoacyl-tRNA Synthetase and its Interaction with Related tRNA | |
| 2002 | Recombinant Human Epidermal Growth Factor | National Science and Technology Progress Award ($2^{nd}$ grade) |

From 2009 to 2011, SIBCB succeeded in attracting 184 extramural research grants from the Ministry of Science and Technology (MOST), National Natural Science Foundation of China (NSFC), Chinese Academy of Sciences (CAS) and Science and Technology Commission of Shanghai Municipality (STCSM), with a total contract sum of ¥ 373 million.




## Major National Research Grants (2009-2011)

| Year | Title | Classification | PI |
|---|---|---|---|
| 2011 | Cell lineage Establishment and Developmental Regulation | CAS "Stem Cell and Regenerative Medicine" Strategic Priority Research Program (Stem Cell SPRP) | Naihe Jing |
| 2009 | Signaling of Cell-Cell Interaction during Inflammation: Mechanism and Application | MOST National Basic Resarch Program (973 Program) | Jianfeng Chen |
| 2011 | Molecular Mechanism of Inflammation-Driven Cancer | MOST Key Science Research Program | Anning Lin |
| 2011 | Mechanisms of Epithelial Tissue Formation, Renewal and Regulation | | Xueliang Zhu |
| 2010 | Subcellular Metabolism Regulation and Mechanism of Related Diseases such as Senile Dementia | | Boliang Li |
| 2010 | Study of Structural Biology Technologies and Methods Based on Shanghai Synchrotron Radiation Facility | | Rongguang Zhang |
| 2010 | Molecular Mechanism and Structural Basis of Epigenetic Regulation during Stem Cell Programming and Reprgramming | | Jianping Ding |
| 2009 | Function and Mechanism of Important Protein Groups Involved in Cell Growth Regulation | | Lin Li |



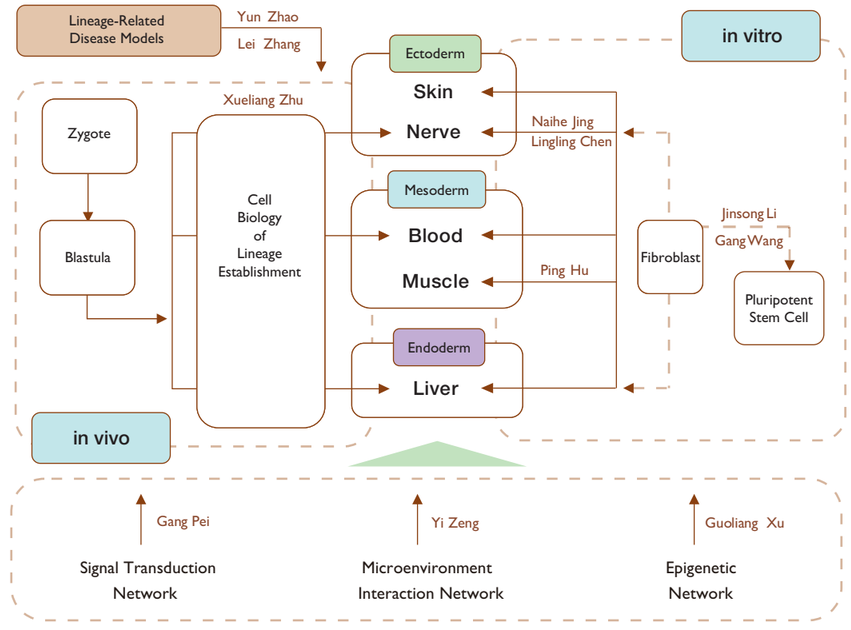


## Stem Cell SPRP

The "Stem Cell and Regenerative Medicine" Strategic Priority Research Program (Stem Cell SPRP) is the only SPRP in biological sciences among the first batch of SPRPs launched by Chinese Academy of Sciences. As an important part of the CAS "Innovation 2020" Strategic Plan, the phase I of Stem Cell SPRP is a five-year program (2011-2015) with a total budget of ¥ 920 million.

SIBCB is actively engaged in the implementation of Stem Cell SPRP, with Prof. Naihe Jing acting as the chief scientist of project 1 "Cell Lineage Establishment and Developmental Regulation" and 13 PIs undertaking the research work of project 1, 2, and 4. Since the launch of the Program, SIBCB participating scientists has made outstanding progress in stem cell research with publications in *Nature* (2), *Science* (1), *Cell Stem Cell* (1), *Developmental Cell* (1), *Molecular Cell* (1) and *Nature Cell Biology* (1) (by the end of July, 2012).

### Project 1 Cell Lineage Establishment and Developmental Regulation




Project 1 research outline

### Project 2 Core Technologies for Obtaining Functional Cells

Sub-Project 3 Prof. Lijian Hui

### Project 4 Integrated Study of Stell Cell Application Strategies

Sub-Project 4 Prof. Degui Chen

# Core Facilities

At the end of May 2012, the SIBCB Center of Core Facilities has 5 senior technicians, 21 middle-level technicians and 35 junior technicians,who manage 7 core facilities with equipment worth more than ¥ 90 million.

## Molecular Biology Core Facility

Nucleic Acid Analysis
Biomolecular Interaction Analysis
Molecular Imaging
Spectrometry
Chromatography
Nuclear Magnetic Resonance Spectroscopy
Mass Spectrometry

## Cell Biology Core Facility

Laser Scanning Confocal Microscopy
Fluorescent Microscopy
Live Cell Imaging
Flow Cytometry
Electron Microscopy

## Chemical Biology Core Facility

High-Throughput Screening of Small Molecule Libraries
Genome-Wide RNAi Screening

## Stem Cell Core Facility

Embryonic Stem Cell Line Establishment
Mouse/Cell Gene Modifications
Tests and Essays
Histological Analysis





## Animal Core Facility

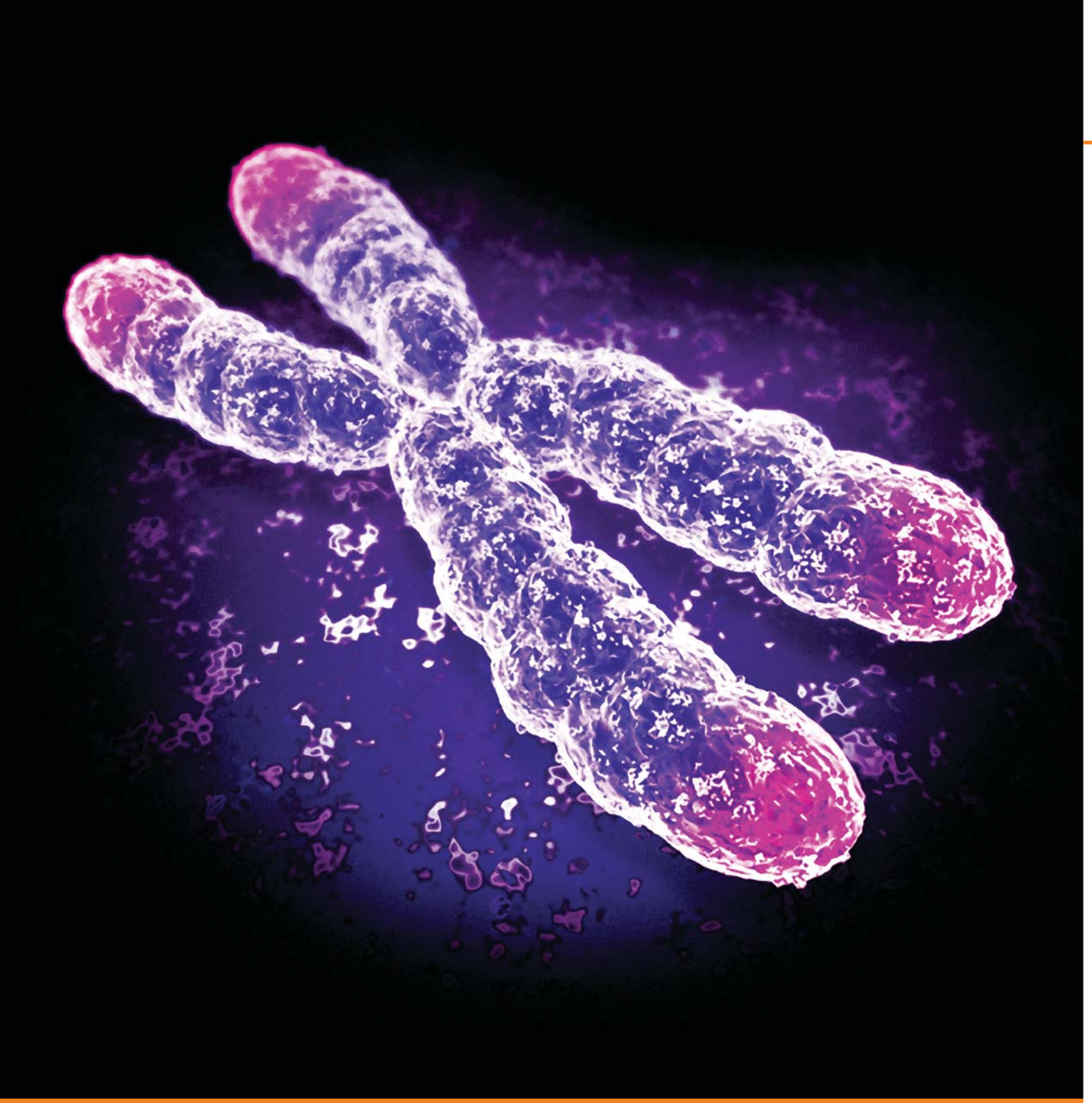
Animal Care
Imaging Analysis
Behavior Analysis
Embryo Manipulation
Transgenesis

## Fruit Fly Core Facility

Strain Introduction and Maintenance
Mutant Strain Exchange and Preparation
Gene Cloning
Microinjection

## Zebrafish Core Facility

Strain Introduction and Maintenance
Transgenesis and Gene Knock-Out
Stereo Fluorescence Microscope
Embryo Microinjection



# Research Highlights

## Gene Regulation, RNA and Epigenetics

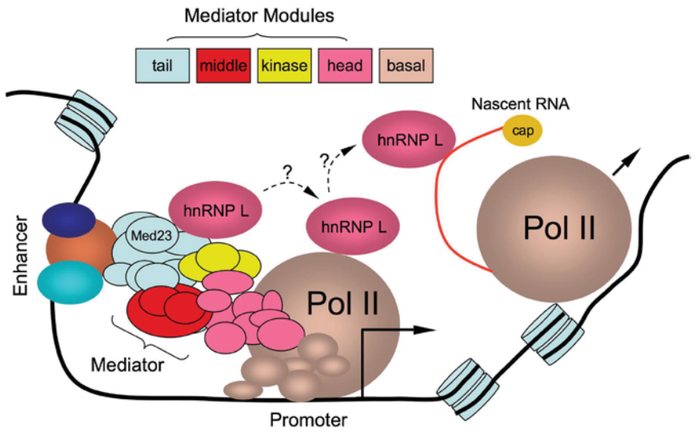
Gene Regulation
RNA Biology
DNA Methylation
Histone Modification
Telomere Biology



### 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.

Reference: 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]

#### Selected Reading

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

#### Further Reading

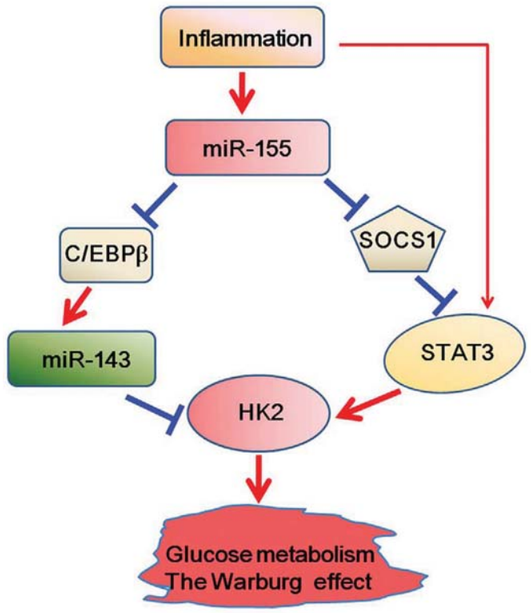
Lei L, Xiong Y, Chen J, Yang JB, Wang Y, Yang XY, Chang CC, Song BL, Chang TY, Li BL (2009) TNF-alpha stimulates the ACAT1 expression in differentiating monocytes to promote the CE-laden cell formation. *J. Lipid Res.* 50:1057-67.

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

## 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.
Reference: 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.

### Selected Reading

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

### Further Reading

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]

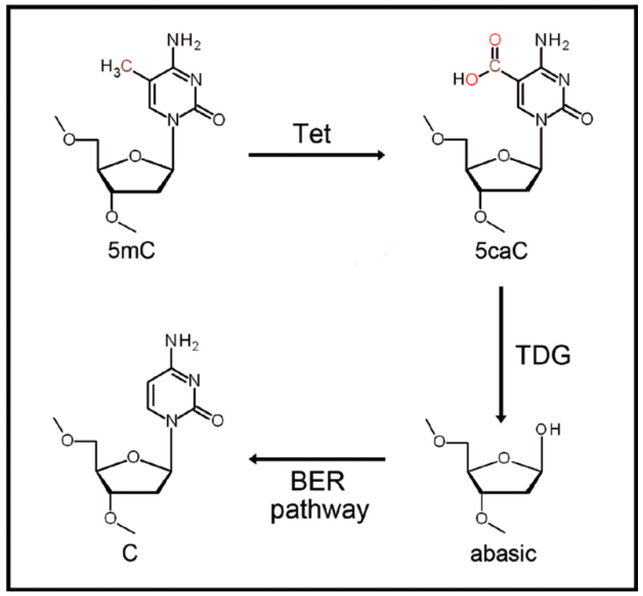
Piao X, Zhang X, Wu L#, Belasco JG# (2010) CCR4-NOT deadenylates mRNA associated with





## 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.
Reference: 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.

### Selected Reading

Gu TP*, Guo F*, Yang H*, Wu HP, Xu GF, Liu W, Xie ZG, Shi L, He X, Jin SG, Iqbal K, Shi YG, Deng Z, Szabó PE, Pfeifer GP, Li J#, Xu GL# (2011) The role of Tet3 DNA dioxygenase in epigenetic reprogramming by oocytes. *Nature* 477:606-610

Hu JL, Zhou BO, Zhang RR, Zhang KL, Zhou JQ#, Xu GL# (2009) The N-terminus of histone H3 is required for de novo DNA methylation in chromatin. *Proc. Natl. Acad. Sci. U S A* 106:22187-192

### Further Reading

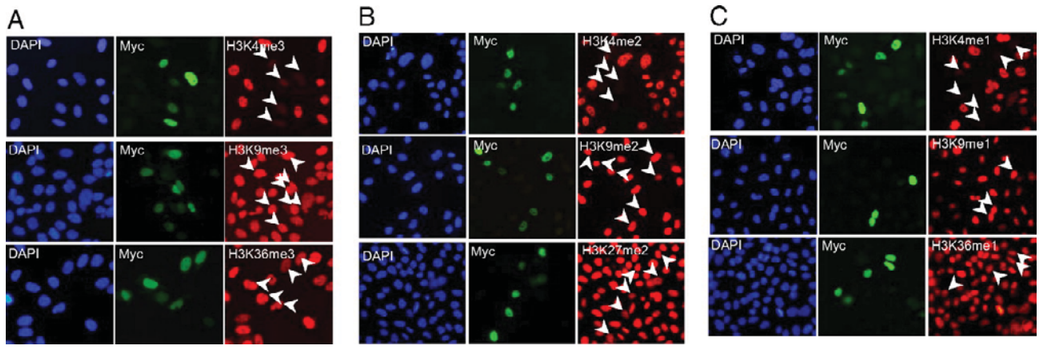
Liu P*, Nie S*, Li B, Yang ZQ, Xu ZM, Fei J, Lin C, Zeng R, Xu GL (2010) Deficiency in a glutamine-specific methyltransferase for the release factor causes mouse embryonic lethality. *Mol. Cell. Biol.* 30:4245-53

Shen L, Gao G#, Zhang Y, Zhang H, Ye Z, Huang S, Huang J, Kang J# (2010) A single amino acid substitution confers enhanced methylation activity of mammalian Dnmt3b on chromatin DNA. *Nucleic Acids Res.* 38:6054-64

## 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.

Reference: Xiang et al. (2007) *Proc. Natl. Acad. Sci. U S A* 104:19226-31




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.

### Selected Reading

Zhou BO, Wang SS, Zhang Y, Fu XH, Dang W, Lenzmeier BA, Zhou JQ (2011) Histone H4 lysine 12 acetylation regulates telomeric heterochromatin plasticity in *Saccharomyces cerevisiae*. *PLoS Genet.* 7:e1001272

Lin YH, Kakadia PM, Chen Y, Li YQ, Deshpande AJ, Buske C, Zhang KL, Zhang Y, Xu GL#, Bohlander SK# (2009) Global reduction of the epigenetic H3K79 methylation mark and increased chromosomal instability in CALM-AF10–positive leukemias. *Blood* 114:651-658

### Further Reading

Wang SS, Zhou BO#, Zhou JQ# (2011) Histone H3 lysine 4 hypermethylation prevents aberrant nucleosome remodeling at the PHO5 promoter. *Mol. Cell. Biol.* 31:3171-81

Zhu Z, Wang Y, Li X, Wang Y, Xu L, Wang X, Sun T, Dong X, Chen L, Mao H, Yu Y, Li J, Chen PA#, Chen CD# (2010) PHF8 is a histone H3K9me2 demethylase regulating rRNA synthesis. *Cell Res.* 20:794-801

Liu B, Lin Y, Darwanto A, Song X, Xu G#, Zhang K# (2009) Identification and characterization of propionylation at histone H3 lysine 23 in mammalian cells. *J. Biol. Chem.* 284:32288-95

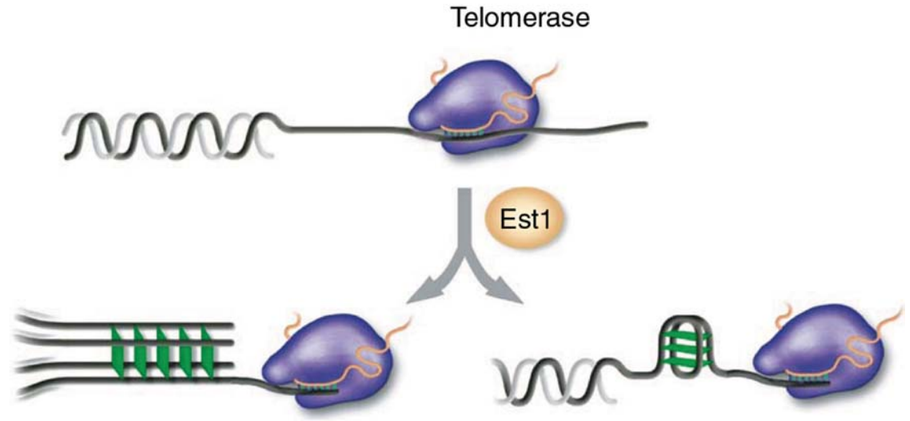




## Yeast telomerase subunit Est1p is required for telomere elongation

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.

Reference: Zhang et al. (2010) *Nat. Struct. Mol. Biol.* 17:202-209




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.

### Selected Reading

Chen XF, Meng FL, Zhou JQ (2009) Telomere recombination accelerates cellular aging in *Saccharomyces cerevisiae*. *PLoS Genet.* 5:e1000535

Meng FL, Hu Y, Shen N, Tong XJ, Wang J, Ding J, Zhou JQ (2009) Sua5p a single-stranded telomeric DNA-binding protein facilitates telomere replication. *EMBO J.* 28:1466-78

### Further Reading

Peng J, Zhou JQ (2012) The tail-module of yeast Mediator complex is required for telomere heterochromatin maintenance. *Nucleic Acids Res.* 40:581-593

Tong XJ, Li QJ, Duan YM, Liu NN, Zhang ML, Zhou JQ (2011) Est1 protects telomeres and inhibits subtelomeric Y'-element recombination. *Mol. Cell. Biol.* 31:1263-74

Zhou BO, Wang SS, Xu LX, Meng FL, Xuan YJ, Duan YM, Wang JY, Hu H, Dong X, Ding J, Zhou JQ (2010) SWR1 complex poises heterochromatin boundaries for antisilencing activity propagation. *Mol. Cell. Biol.* 30:2391-2400

# Research Highlights

## Protein Science

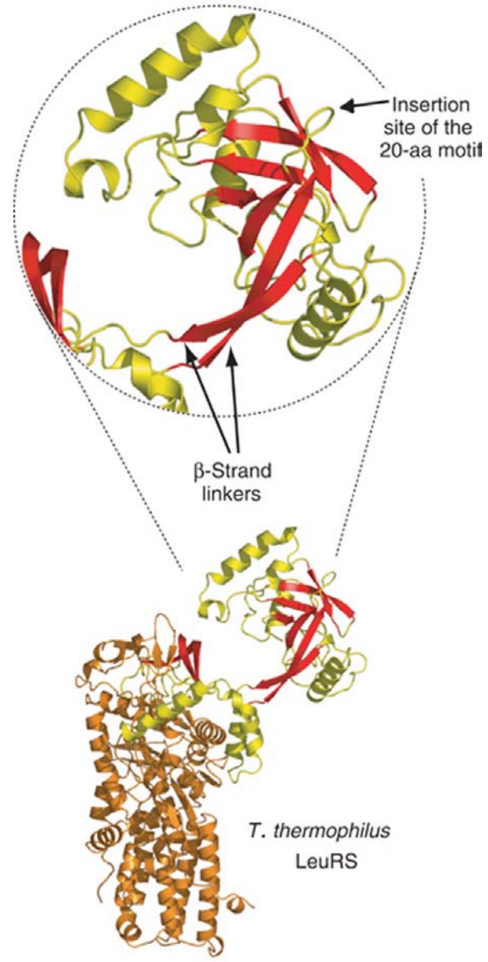
Protein Biosynthesis and Degradation
Protein Structural Biology
Proteomics



## 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.

Reference: Zhao et al. (2005) *EMBO J.* 24:1430-39




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.

### Selected Reading

Hu RG, Wang H, Xia Z, Varshavsky A (2008) The N-end rule pathway is a sensor of heme. *Proc. Natl. Acad. Sci.* U S A 105:76-81

### Further Reading

Protein Biosynthesis

Zhou XL, Du DH, Tan M, Lei HY, Ruan LL, Eriani G, Wang ED (2011) Role of tRNA amino acid-accepting end in aminoacylation and its quality control. *Nucleic Acids Res.* 39:8857-68

Huang S, Lin Q (2003) Functional expression and processing of rat choline dehydrogenase precursor. *Biochem. Biophys. Res. Commun.* 309:344-50

Protein Degradation

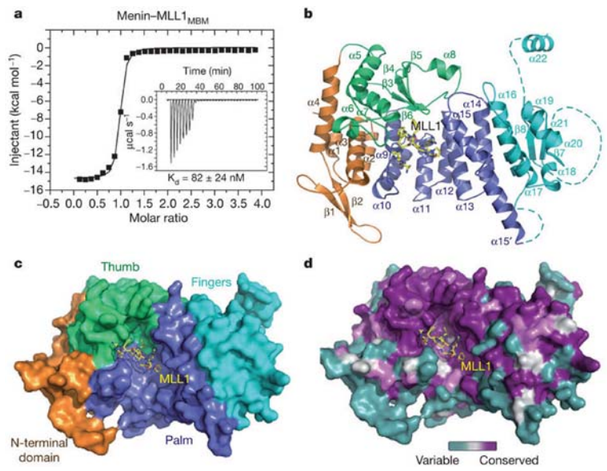
Gao XC, Zhou CJ, Zhou ZR, Zhang YH, Zheng XM, Song AX, Hu HY (2011) Co-chaperone HSJ1a dually regulates the proteasomal degradation of *ataxin-3*. *PLoS One* 6:e19763

Fu QS, Zhou CJ, Gao HC, Jiang YJ, Zhou ZR, Hong J, Yao WM, Song AX, Lin DH#, Hu HY# (2009) Structural basis for ubiquitin recognition by a novel domain from human phospholipase $A_2$-activating protein. *J. Biol. Chem.* 284:19043-52

## 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.

Reference: Huang et al. (2012) *Nature* 482:542-6




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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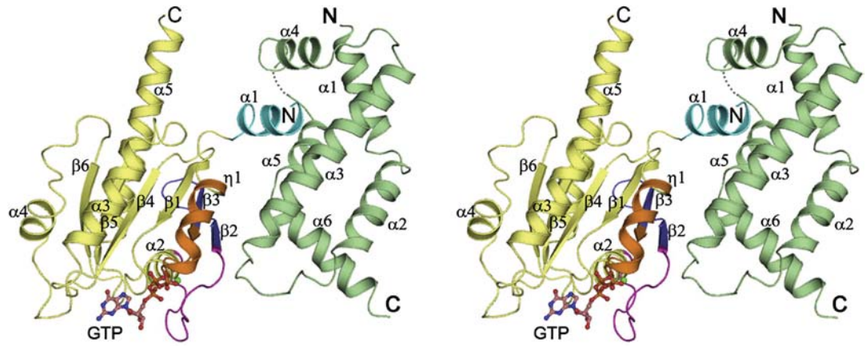
## ARL2-GTP-BART structure reveals a novel mode of GTPase-effector binding

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.

Reference: Zhang et al. (2009) *Structure* 17:602-610




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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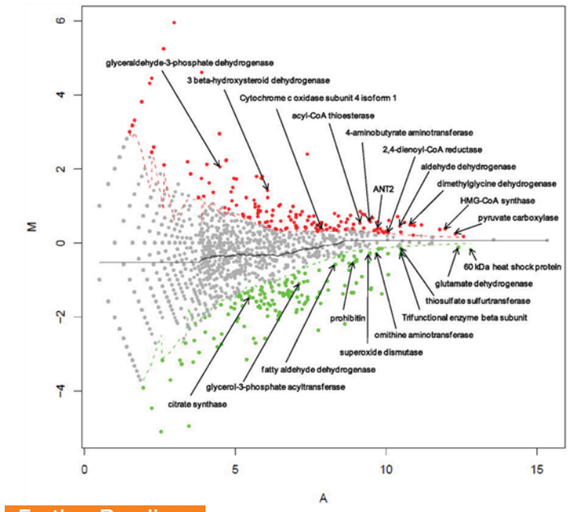
## Proteomic characterization of liver mitochondria in diabetic rats

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.

Reference: Deng et al. (2010) *Mol. Cell. Proteomics* 1:100-116




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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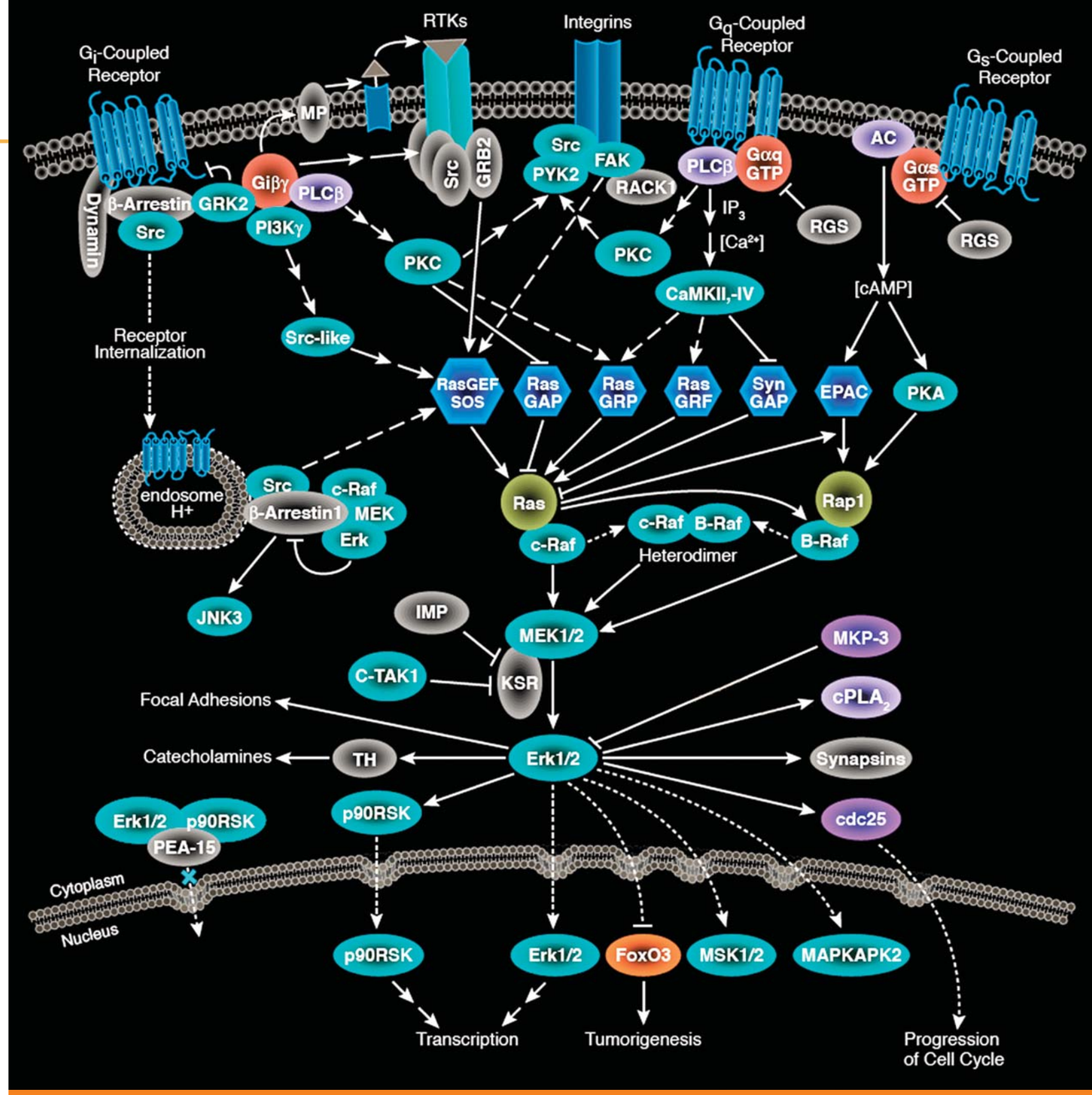


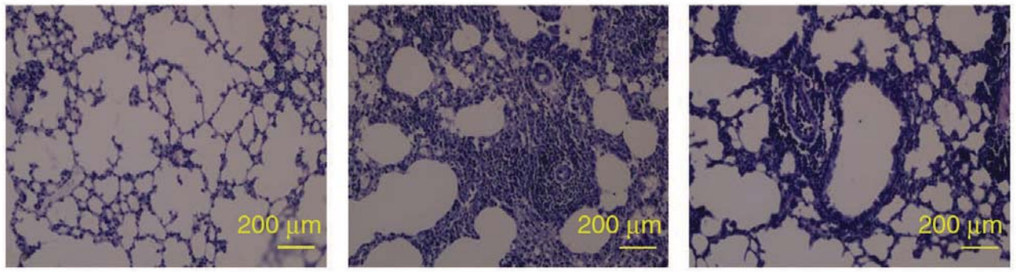

# Research Highlights

## Cellular Signal Transduction

- Immune Signaling
- GPCR/β-Arrestin Signaling
- Wnt Signaling
- NF-κB Signaling
- TNF-α Signaling

## 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.
Reference: Li et al. (2011) *Nat. Immunol.* 12:178-185




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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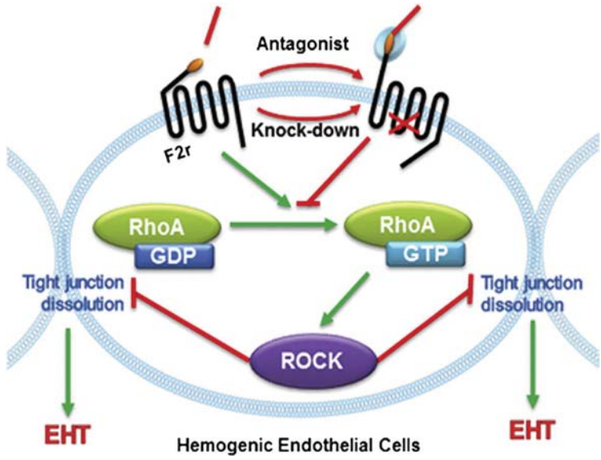
## Thrombin receptor regulates endothelial-to-hematopoietic transition

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.
Reference: Yue et al. (2012) *Dev. Cell* 139:535-546




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.

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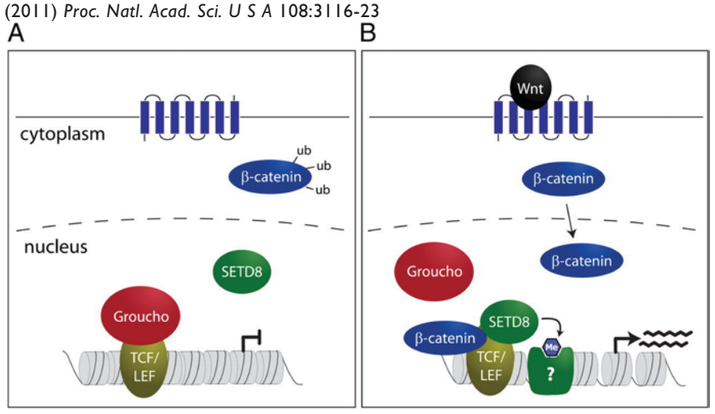
## H4K20 monomethylation mediates Wnt target gene activation

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.

Reference: Li et al. (2011) *Proc. Natl. Acad. Sci. U S A* 108:3116-23




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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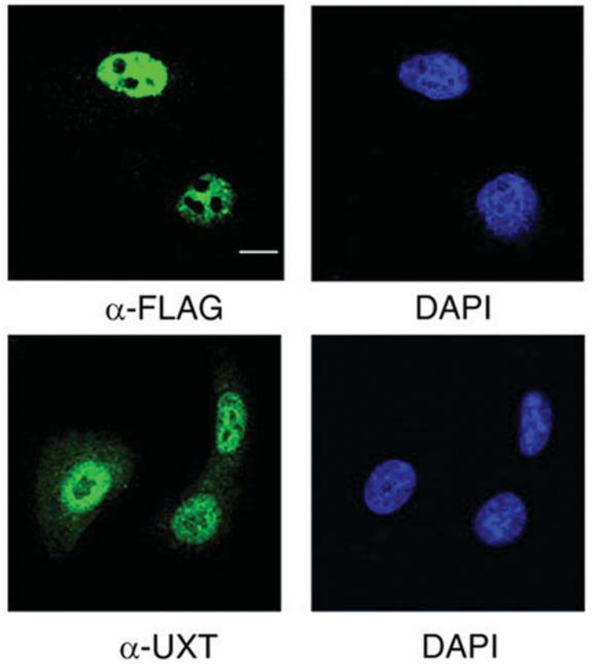
## UXT: An essential cofactor of the NF-κB enhanceosome

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.

Reference: Sun et al. (2007) *J. Cell Biol.* 178:231-244




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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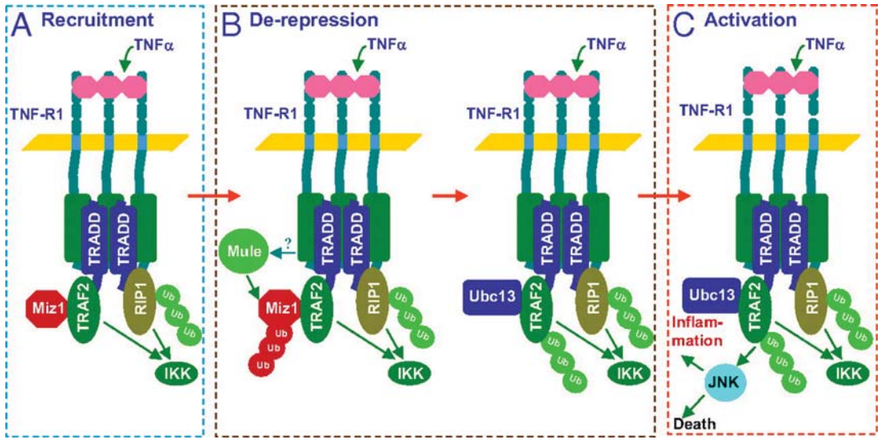
## Miz1 degradation is required for relieving its suppression on TNF-α induced JNK activation

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.

Reference: Liu et al. (2012) *Proc. Natl. Acad. Sci. U S A* 109:191-196




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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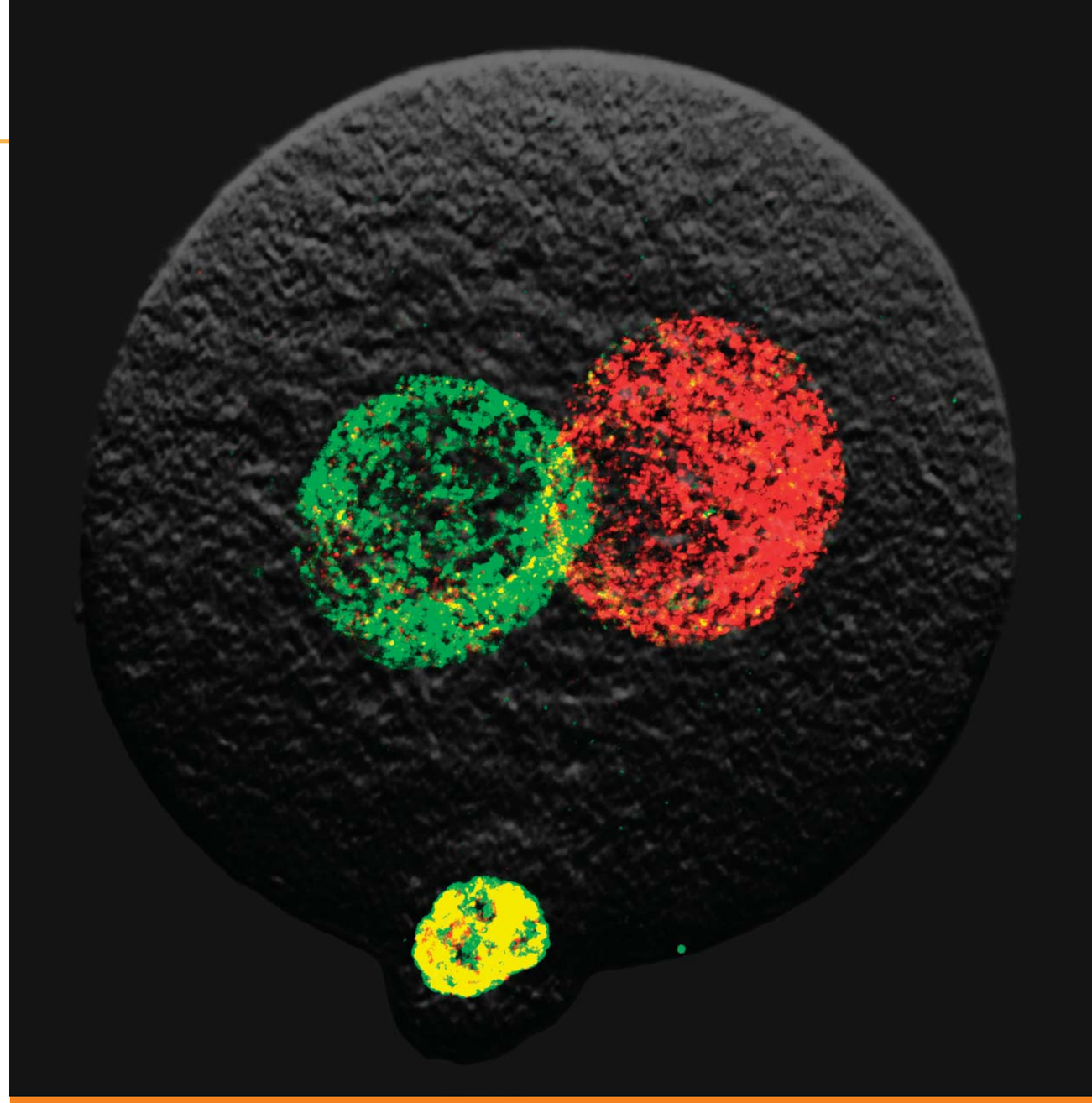


# Research Highlights

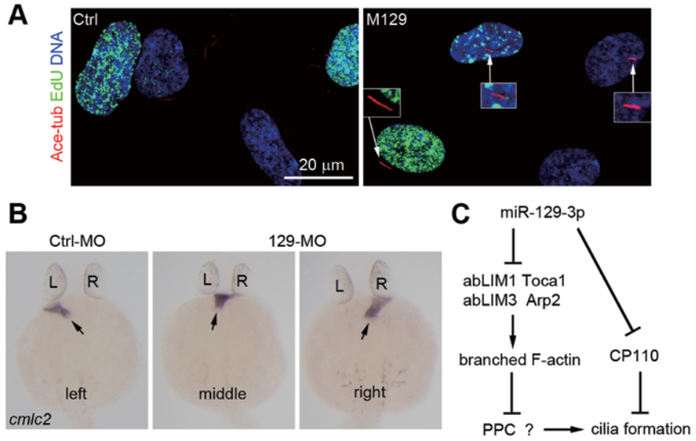
## Cell and Stem Cell Biology

Motility and Apoptosis
Differentiation and Development
Stem Cell Biology
Reproductive Biology
Neural Biology

## 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.

Reference: Cao et al. (2012) *Nat. Cell Biol.* 14:697–706




(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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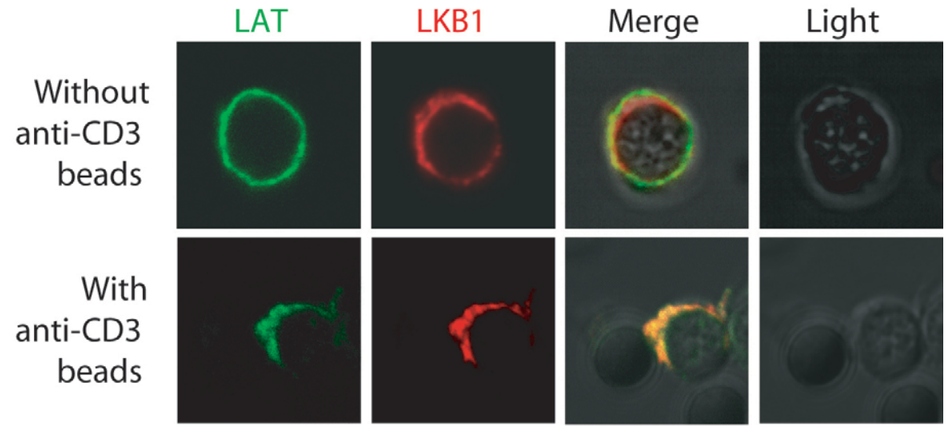
## LKB1 plays a critical role in thymocyte development

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.

Reference: Cao et al. (2011) *EMBO J.* 30:2083-93




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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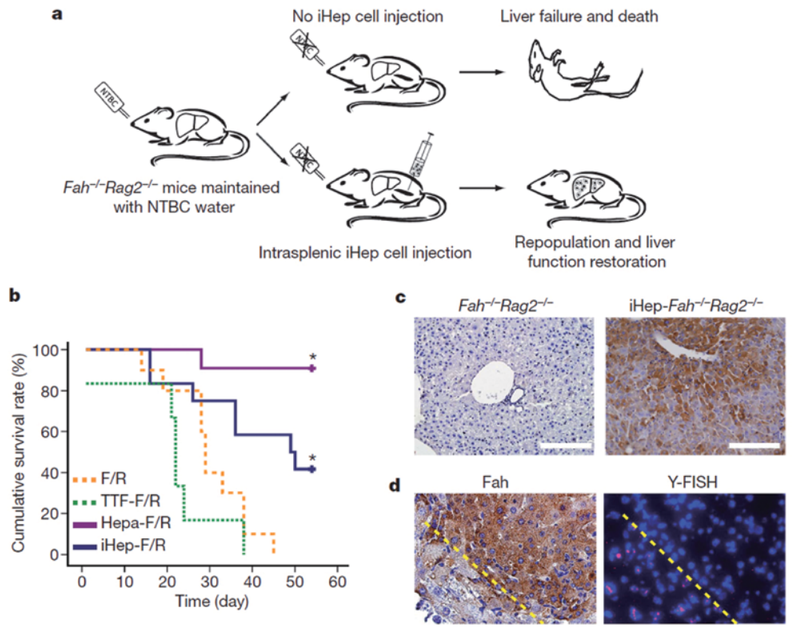
## Direct conversion of mouse fibroblasts to functional hepatocyte-like cells

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.

Reference: Huang et al. (2011) *Nature* 475:386-389




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.





## 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.

Reference: Yang et al. (2012) *Cell* 149:605-617

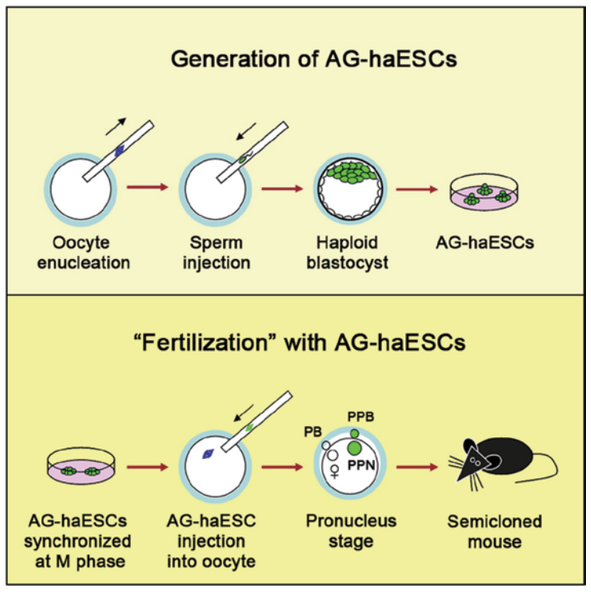



Diagram showing the generation of AG-haESCs (top) and "fertilization" of oocytes with AG-haESCs (bottom).

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Hu P, Geles KG, Paik JH, DePinho RA, Tjian R (2008) Codependent activators direct myoblast-specific MyoD transcription. *Dev. Cell* 15:534-46

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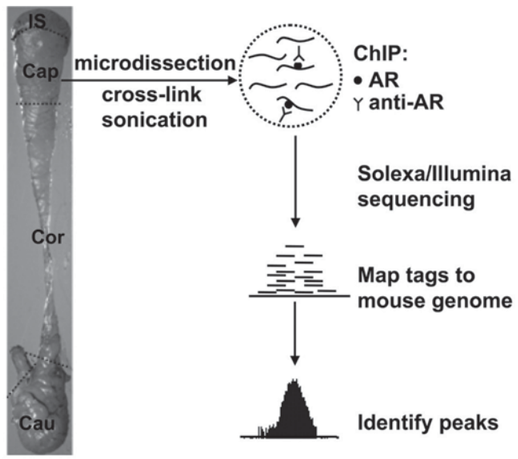
Chen T*, Yuan D* , Wei B, Jiang J, Kang J, Ling K, Gu Y, Li J, Xiao L, Pei G (2010) E-cadherin-mediated cell-cell contact is critical for induced pluripotent stem cell generation. *Stem Cells* 28:1315-25

## 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.

Reference: Hu et al. (2010) *Mol. Endocrinol.* 24:2392-405




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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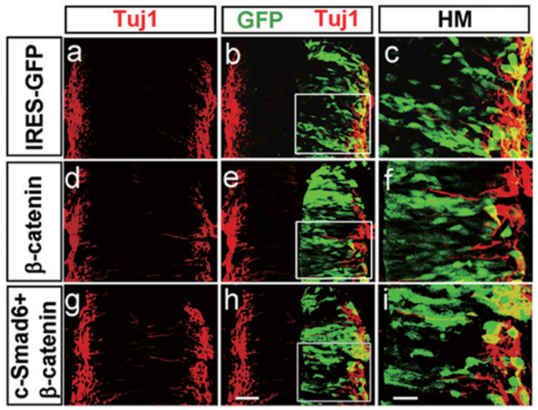
## Smad6 promotes neuronal differentiation by inibiting Wnt signaling

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.

Reference: Xie et al. (2011) *Proc. Natl. Acad. Sci. U S A* 108:12119-24




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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# Research Highlights

## Cancer and Other Diseases

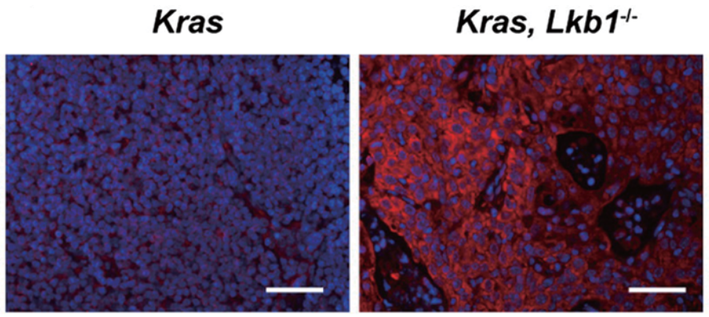
- Cancer Biology
- Molecular Cancer Medicine
- Metabolic Diseases
- Neurodegenerative Diseases
- Liver Diseases



## 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.

Reference: Gao et al. (2010) *Proc. Natl. Acad. Sci. U S A* 107:18892-7




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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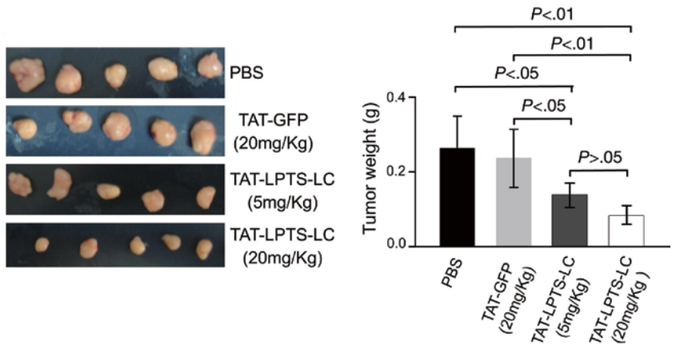
## TAT-LPTS-LC: A potential protein-based anticancer agent

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.

Reference: Chen et al. (2011) *Gastroenterology* 140:332-43




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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## 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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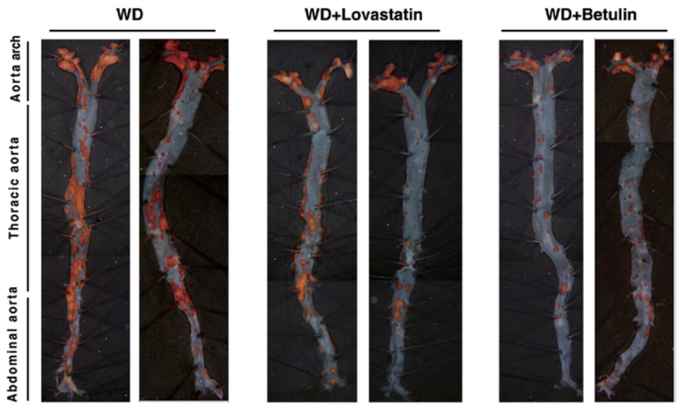


Treatment of betulin decreases atherosclerosis in $LDLR^{-/-}$ mice. Eight-week-old male $LDLR^{-/-}$ mice were randomly grouped and fed with WD supplemented with vehicle (n = 7), 30 mg/kg/day of lovastatin (n = 3), or 30 mg/kg/day of betulin (n = 6) for 14 weeks. Blood samples were collected 3 days 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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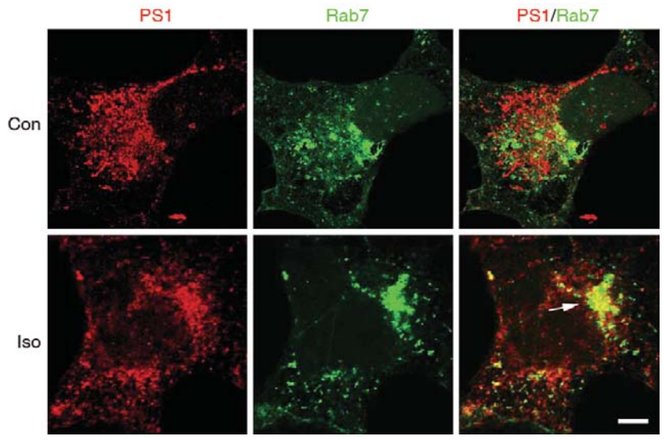
## Abnormal activation of $\beta_2$-AR may contribute to Alzheimer disease pathogenesis

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.

Reference: Ni et al. (2006) *Nat. Med.* 12: 1390-96




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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Xie YY, Zhou CJ, Zhou ZR, Hong J, Che MX, Fu QS, Song AX, Lin DH, Hu HY (2010) Interaction with synphilin-1 promotes inclusion formation of α-synuclein: mechanistic insights and pathological implication. *FASEB J.* 24:196-205

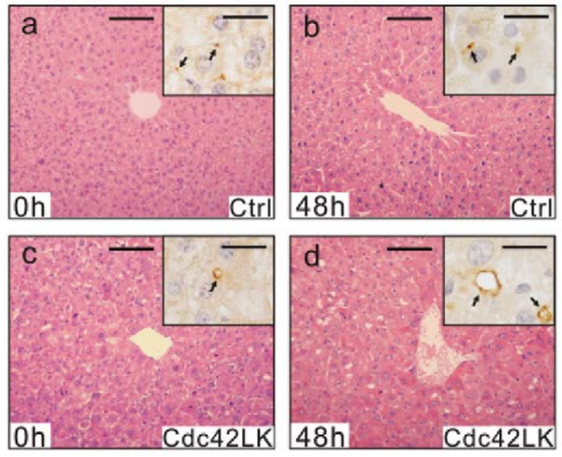




## Cdc42 regulates proliferative signaling during liver regeneration

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.

Reference: Yuan et al. (2009) *Hepatology* 49:240-249




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.

### Further Reading

Lu X#, Feng X#, Man X, Yang G, Tang L, Du D, Zhang F, Yuan H, Huang Q, Zhang Z, Liu Y, Strand D, Chen Z (2009) Aberrant splicing of *Hugl-1* Is associated with hepatocellular carcinoma progression. *Clin. Cancer Res.* 15:3287-96

### Selected Reading

Chen YL, Lv J, Ye XL, Sun MY, Xu Q, Liu CH, Min LH, Li HP, Liu P#, Ding X# (2011) Sorafenib inhibits transforming growth factor β1-mediated epithelial-mesenchymal transition and apoptosis in mouse hepatocytes. *Hepatology* 53:1708-18

Pan X, Wang X, Lei W, Min L, Yang Y, Wang X, Song J (2009) Nitric oxide suppresses transforming growth factor-β1-induced epithelial-to-mesenchymal transition and apoptosis in mouse hepatocytes. *Hepatology* 50:1577-87

Tang H, Da L, Mao Y, Li Y, Li D, Xu Z, Li F, Wang Y, Tiollais P, Li T, Zhao M (2009) Hepatitis B virus X protein sensitizes cells to starvation-induced autophagy via up-regulation of beclin 1 expression. *Hepatology* 49:60-71

## Intellectual Property

From 2009 to 2011, SIBCB scientists filed 102 patent applications including 14 international patent applications, and got 54 granted patents including 5 international patents.

## International Patents (2009-2011)

| Patent Number | Patent Name | Date Issued | Inventors |
|---|---|---|---|
| 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 angiogenesis 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 |





## Technology Transfer

From 2009 to 2011, SIBCB signed 6 patent licensing contracts with biomedical companies, with a total contract sum of ¥ 417 million.

In 2010, "Detection and modulation of Slit and Robo mediated angiogenesis and uses thereof", an SIBCB researchers' invention, was successfully transferred to Sanofi-Aventis with a contract sum of $ 60 million.

From 2009 to 2011, SIBCB established 7 collaborative research / technology transfer / commissioned research projects with biomedical companies, with a total contract sum of ¥ 10.3 million.

In 2011, SIBCB established strategic partnership with Shandong Yikang Pharmaceutical Co., Ltd. to jointly develop EFE-6 (earthworm fibrinolytic enzyme-6), a national first-grade biotech drug originated from an invention made by SIBCB scientists.


In 2009, SIBCB established a joint cancer research center with Shanghai Xuhui District Central Hospital (SXDCH) to conduct translational cancer research. Buiding on the success of the SIBCB-SXDCH partnership, SIBCB is now working with Eastern Hepatobiliary Surgery Hospital to set up another cancer research center. SIBCB also formed strong collaboration relationship with Shanghai Pulmonary Hospital, Shanghai Chest Hospital, Shanghai Tumor Hospital, and Shanghai Xinhua Hospital.

# Scientific Publishing


## Cell Research

Editor-in-Chief

Prof. Gang Pei

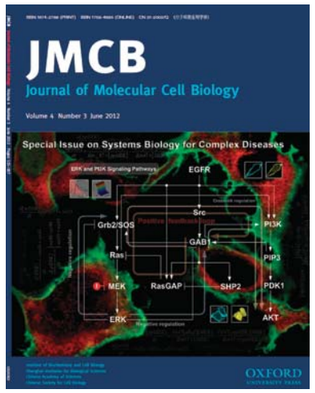
Journal Profile

*Cell Research* is a peer-reviewed international journal publishing results in all disciplines of cell biology and molecular biology. Launched in 1990, *Cell Research* is currently sponsored by SIBCB and published monthly by Nature Publishing Group (NPG). With its 2011 impact factor of 8.190, *Cell Research* is ranked 23rd among 180 SCI-indexed cell biology journals, and 1st among 154 SCI-indexed Chinese journals.

Journal Website

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

http://www.nature.com/cr/index.html




## Journal of Molecular Cell Biology

Editor-in-Chief

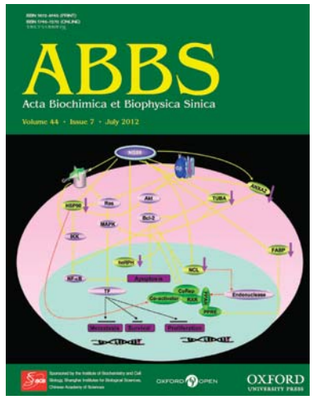
Prof. Jiarui Wu

Journal Profile

*Journal of Molecular Cell Biology (JMCB)* is an online, peer-reviewed international journal interested in inter-disciplinary studies at the cross-sections between molecular and cell biology as well as other disciplines of life sciences. Launched in 2009, *JMCB* is currently co-sponsored by SIBCB and published bimonthly by Oxford University Press. With its 2011 impact factor of 7.667, *JMCB* is ranked 28th among 180 cell biology SCI journals.

Journal Website

http://jmcb.oxfordjournals.org/




## Acta Biochimica et Biophysica Sinica

Editor-in-Chief

Prof. Boliang Li

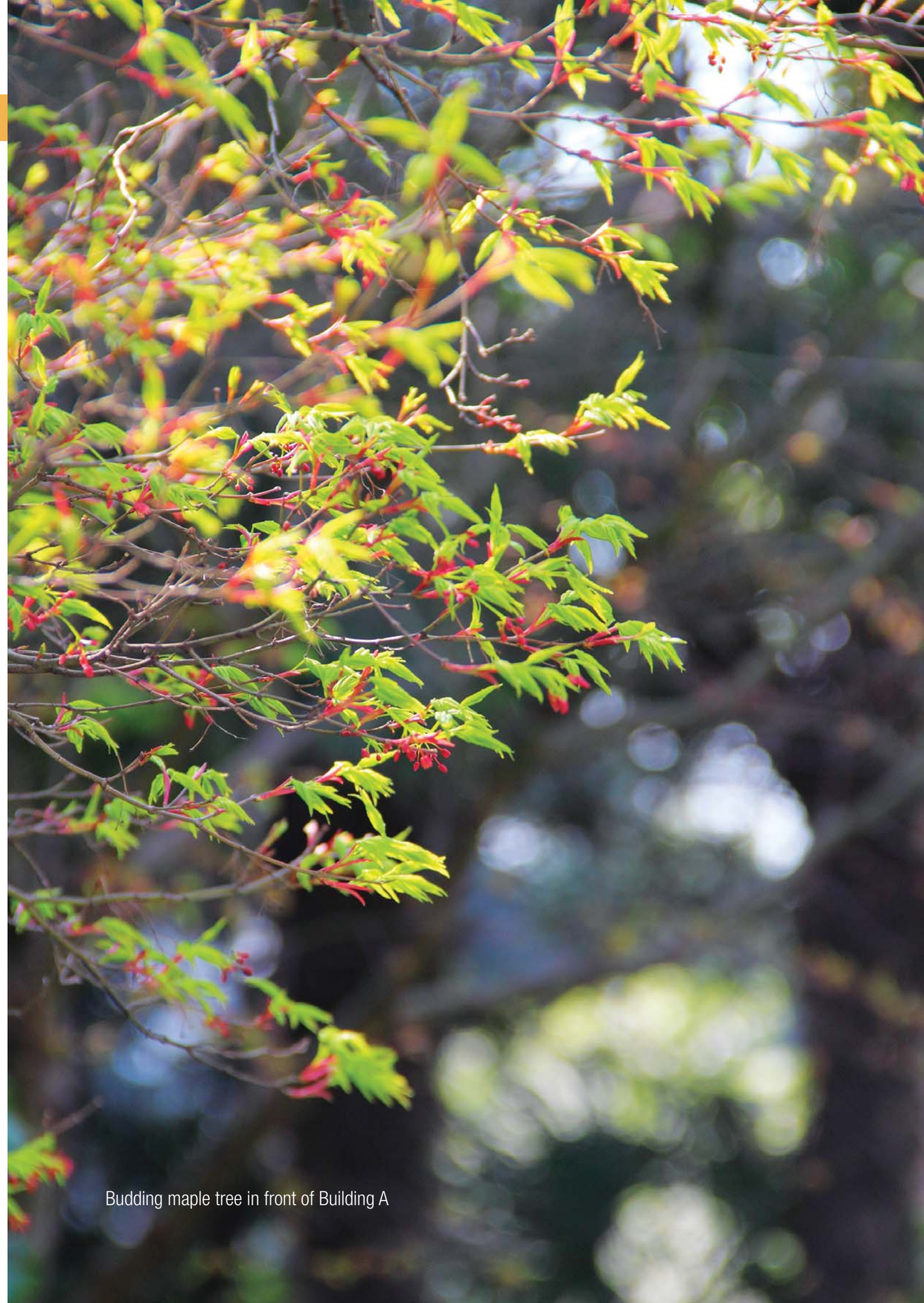
Journal Profile

Acta Biochimica et Biophysica Sinica (ABBS) is a peer-reviewed international journal publishing results in diverse fields of biomedical research. Launched in 1958, ABBS is currently sponsored by SIBCB and published monthly by Oxford University Press. The 2011 impact factor of ABBS is 1.376.

Journal Website

http://www.abbs.info/

http://abbs.oxfordjournals.org/



Budding maple tree in front of Building A

## Major Research Clusters

State Key Laboratory of Molecular Biology

State Key Laboratory of Cell Biology

National Center for Comprehensive Protein Science Shanghai

SIBCB Building B

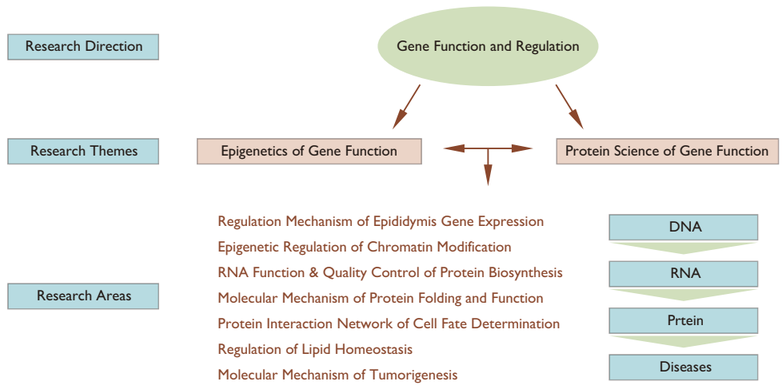
# State Key Laboratory of Molecular Biology

Established in 1987, State Key Laboratory of Molecular Biology (SLMB) is China's first state key laboratory in biological sciences. Targeting the national strategic demand "population and health", SLMB conducts innovative research in biochemistry and molecular biology, and aims at 1) developing into an internationally competent research laboratory, 2) contributing to the prevention and treatment of diseases.

**Prof. Lin Li**
Director
CAS Member

**Prof. Yunyu Shi**
Academic Committee Chairperson
CAS Member

## Academic organization




## Faculty

At the end of May, 2012, SLMB has 29 PIs including 5 CAS members, 2 TTP scholars, 7 NSFDYS recipients, and 15 HTP scholars.

## Publications

From 2009 to 2011, SLMB researchers published 148 SCI articles including 81 IF≥5 articles and 11 IF≥10 articles, and the average IF is 7.3.

## Patents

From 2009 to 2011, SLMB researchers filed 28 patent applications, and got 20 patents.

## Awards / Honors

"Revealing the Important Role of Tet Dioxygenases in Mammalian Epigenetic Regulation" was selected as one of the "Top 10 Achievements of Chinese Science" in 2011.



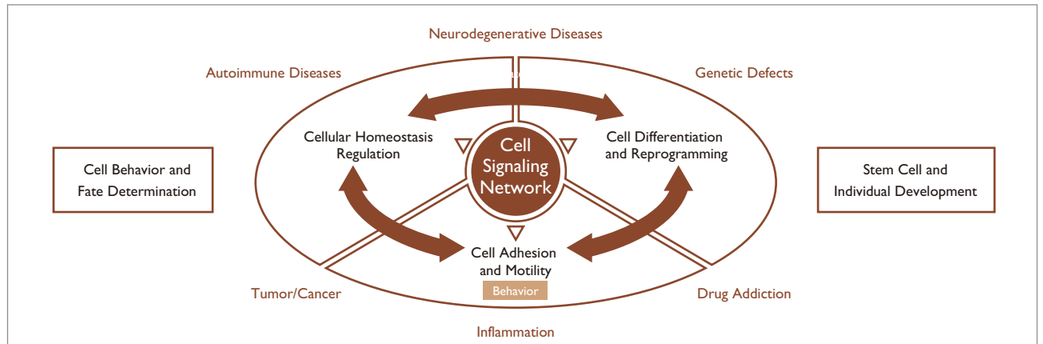
# State Key Laboratory of Cell Biology

After the official approval by Ministry of Science and Technology in October 2011, SIBCB started the pre-launch development of State Key Laboratory of Cell Biology based on the CAS Laboratory of Cell Biology established in 1997, and expects to complete the project within two years. SKLCB aims at 1) conducting high-standard basic and translational research in cell biology and stem cell biology, 2) providing innovative scientific findings and technological support to address the national strategic demand "population and health", and 3) developing into an internationally competent research laboratory.

**Prof. Xueliang Zhu**
Director

**Prof. Hongyang Wang**
Academic Committee Chairperson
CAE Member

## Academic organization




## Faculty

At the end of May, 2012, SKLCB has 28 PIs including 3 CAS members, 1 TTP scholars, 8 NSFDYS recipients, and 19 HTP scholars.

## Publications

From 2009 to 2011, SKLCB researchers published 118 SCI articles including 79 IF≥5 articles and 17 IF≥10 articles, and the average IF is 7.8.

## Patents

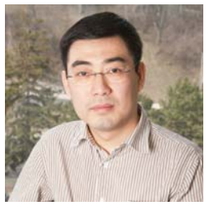
From 2009 to 2011, SKLCB researchers filed 48 patent applications, and got 18 patents.

## Awards / Honors

"Successfully Converting Mouse Fibroblasts to Functional Hepatocyte-like Cells" was selected as one of the "Top 10 Achievements of Chinese Science" in 2011, and "Deficiency of a β-Arrestin-2 Signal Complex Contributes to Insulin Resistance" was selected as one of the "Top 10 News of Chinese Basic Research " in 2009.

National Center for Comprehensive Protein Science Shanghai (NCPS Shanghai) is the in-house research team of the National Facility for Protein Science in Shanghai (NFPS Shanghai), and is one of the three "clusters" in SIBCB's academic organization. Currently located in the Yueyang campus of SIBCB, NCPS Shanghai is deeply engaged in NFPS Shanghai construction and faculty/staff recruitment. By the end of 2012, NCPS Shanghai will gradually move into the newly-built NFPS Shanghai in Zhangjiang Innopark. The main functions of NCPS Shanghai will include: 1) operating NFPS Shanghai and providing excellent support services to all scientists, 2) conducting cutting-edge basic research and technology development in protein science, and 3) promoting translational research and technology transfer.

## Principal Officers



### Prof. Ming Lei

Director

Prior to NCPS: Associate Professor (tenured),University of Michigan; HHMI Early Career Scientist

### Prof. James Chou

Deputy Director

Prior to NCPS: Associate Professor (tenured), Harvard University

### Prof. Rongguang Zhang

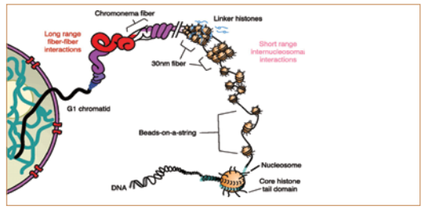
Deputy Director

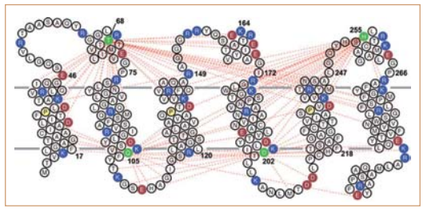
Prior to NCPS: Scientist, Argonne National Laboratory

## Research Areas

### Architecture of Chromosome

Structure, function and regulation of chromosome and related biomacromolecules



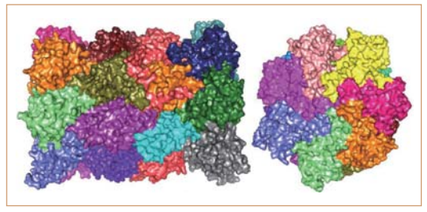



### Biological Processes across Memberane

Transmembrane transport, signaling and cell-cell communication

### Biomacromolecular Machineries

Structure, function and regulation of important biomacromolecular machineries





National Center for Comprehensive Protein Science Shanghai

## National Facility for Protein Science in Shanghai

National Facility for Protein Science in Shanghai (NFPS Shanghai) is China's first national research facility devoted to biological research. Construction started on December 26th, 2010 in Zhangjiang Innopark, Pudong, and is expected to complete at the end of 2013. By then, this ¥ 700 million, 33,550m$^2$, state-of-the-art research facility will be able to provide crystal structure analysis, protein dynamics analysis, and molecular imaging in the beamline stations located within the Shanghai Synchrotron Radiation Facility, and large-scale protein preparation, NMR analysis, cryo-EM analysis, mass spectrometry analysis, compound laser microscopy, molecular imaging and bioinformatic analysis in the SIBCB/NFPS Shanghai Haike campus.


## SIBCB is Responsible for the Construction and Management of NFPS Shanghai

**Engineering & Construction Management Team**

| | | | |
|---|---|---|---|
| Jiarui Wu | Chief Scientist, Vice General Manager | Ming Lei | General Technologist |
| Lin Li | Deputy General Manager | Rongguang Zhang | Deputy General Engineer |
| Naihe Jing | Deputy General Manager, General Engineer | James Chou | Deputy General Technologist |

**Beamline Station Division**

| | |
|---|---|
| Rongguang Zhang | Deputy Director |

**System I: Large-Scale Protein Preparation**

| | |
|---|---|
| Ming Lei | Chief Designer |
| Zhaocai Zhou, Ying Huang | Associate Designers |

**System III: Nuclear Magnetic Resonance Analysis**

| | |
|---|---|
| Hongyu Hu | Chief Designer |
| Chenqi Xu | Associate Designer |

**System IV: Integrated Electron Microscopy Analysis**

| | |
|---|---|
| Naihe Jing | Chief Designer |
| Yao Cong, Yongning He | Associate Designers |

**System VI: Protein Modification and Interaction Analysis**

| | |
|---|---|
| Rong Zeng | Chief Designer |

**System VII: Compound Laser Microscopy**

| | |
|---|---|
| Xueliang Zhu | Chief Designer |
| Wei Bian | Associate Designer |

**System VIII: Molecular Imaging**

| | |
|---|---|
| Xueliang Zhu | Chief Designer |
| Ronggui Hu | Associate Designer |

**Animal Facility**

| | |
|---|---|
| Xiaolong Liu | Chief Designer |
| Haojie Chen | Associate Designer |

# International Collaborations

International Advisory Board

Junior PI Mentor Committee

International Scientific Meetings

International and Regional Partnerships

Other International Activities

21st IUBMB and 12th FAOBMB International Congress of Biochemistry and Molecular Biology (August 2-7th, 2009)

# International Advisory Board

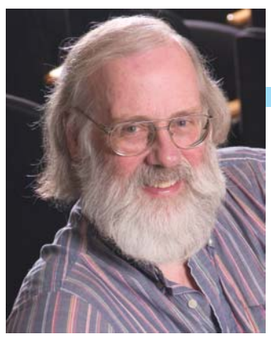
In 2010, SIBCB established its International Advisory Board (IAB) with 7 world renowned scientists as board members. Starting from 2012, IAB will hold regular meetings in SIBCB, and the board members will draw upon their rich academic and administrative experience to help SIBCB build a scholarly research environment and become an internationally renowned institute.

### Sidney Altman, Ph.D.

Sterling Professor, Yale University
Member, National Academy of Sciences, USA
Nobel Laureate, Chemistry, 1989
*Pioneer in RNA research*

### Melanie Cobb, Ph.D.

Professor, University of Texas Southwestern Medical Center
Jane and Bill Browning Jr. Chair in Medical Science
Member, National Academy of Sciences USA
*Pioneer in cell signaling*

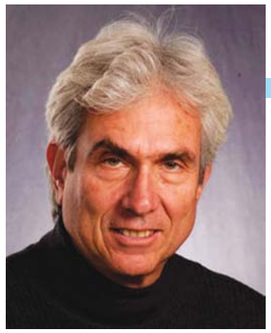


### Tony Hunter, Ph.D.

American Cancer Society Professor, Salk Institute for Biological Studies
Renato Dulbecco Chair in Genomics
Member, National Academy of Sciences, USA
Fellow, the Royal Society, UK
*Discoverer of important protein modifications*







### Michael Karin, Ph.D.

American Cancer Society Professor
Distinguished Professor, University of California San Diego
Member, National Academy of Sciences, USA
*Pioneer in cell signaling and gene regulation*

### Roel Nusse, Ph.D.

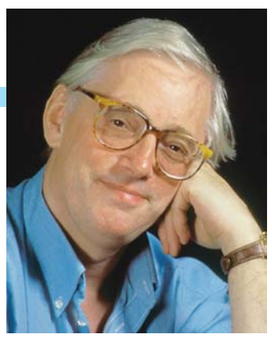
Professor, Stanford University
Howard Hughes Medical Institute Investigator
Member, National Academy of Sciences, USA
*Pioneer in cell signaling and stem cell research*

### Janet Rossant, Ph.D.

Professor, University of Toronto
Lombard Insurance Chair in Paediatric Research
Fellow, the Royal Society, Canada & UK
Foreign Associate, National Academy of Sciences, USA
*Pioneer in developmental biology and stem cell research*

### John Walker, D.Phil.

Professor, University of Cambridge
Fellow, the Royal Society, UK
Foreign Associate, National Academy of Sciences, USA
Nobel Laureate, Chemistry, 1997
*Leading figure in structural biology*

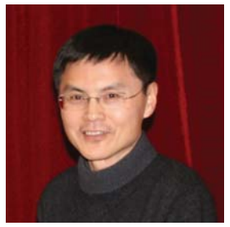


# Junior PI Mentor Committee

Building on the success of the "Signal Transduction" international partnership project, SIBCB set up its junior PI mentor Committee in 2009, the first of its kind among Chinese research institutions. Currently, the Committee consists of 18 renowned overseas and domestic scientists who provide academic mentorship to the Institute's junior PIs, and promote academic exchange between junior PIs and the international academic community.

**Wei Du, Ph.D.**
Professor, University of Chicago

**Xiangdong Fu, Ph.D.**
Professor, University of California San Diego

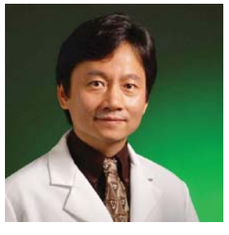


**Hua Gu, Ph.D.**
Professor, McGill University

**Junlin Guan, Ph.D.**
Professor, University of Michigan

**Kunliang Guan, Ph.D.**
Professor, University of California San Diego

**Jiahuai Han, Ph.D.**
Professor, Xiamen University

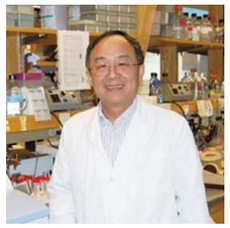


**Haifan Lin, Ph.D.**
Professor, Yale University

**Zhenggang Liu, Ph.D.**
Senior Investigator, National Cancer Institute, NIH



# Junior PI Mentor Committee

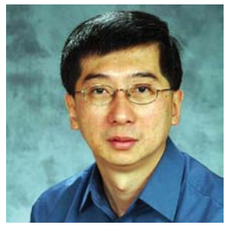


**Shaocong Sun, Ph.D.**
Professor,
University of Texas MD Anderson Cancer Center

**Xiaofan Wang, Ph.D.**
Professor, Duke University

**Dianqing Wu, Ph.D.**
Professor, Yale University

**Hao Wu, Ph.D.**
Professor, Harvard University

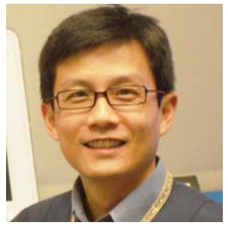


**Ting Xie, Ph.D.**
Professor, Kansas University

**Chi-chung Hui, Ph.D.**
Professor, University of Toronto

**Yingzi Yang, Ph.D.**
Senior Investigator,
National Human Genome Research Institute, NIH

**Wah Chiu, Ph.D.**
Professor, Baylor College of Medicine



**Yixian Zheng, Ph.D.**
Senior Investigator,
Carnegie Institution of Washington

**Heng Zhu, Ph.D.**
Professor, John Hopkins University

# International Scientific Meetings

From 2009 to 2011, SIBCB has organized 20 international scientific meetings, which were attended by more than 4,900 scientists in total. As an important part of SIBCB's global outreach effort, these meetings have been very successful in showcasing SIBCB researchers' work and promoting scientific discussion and collaboration among domestic and overseas scientists.

## The 3rd Shanghai Symposium: Signaling, Inflammation and Cancer

July 25 -28th, 2011

### Organizing Institutions

SIBCB
National Cancer Institute, NIH

### Summary

7 sessions, 43 invited speakers (including 27 overseas speakers) with topics covering mechanisms of cell signaling, cell death and autophagy, signaling and inflammation, signaling and cancer and inflammation and cancer, ~ 400 domestic and overseas participants

## The 4th CAO Tianqin Memorial Symposium on Protein Research

December 5 -8th, 2010


### Organizing Institutions

CAO Tianqin Scholarship Fund
SIBCB
School of Life Sciences, Xiamen University

### Summary

9 sessions, 43 invited speakers (including 23 overseas speakers) with topics covering protein structure and function, porteinases and other enzymes, signal transduction, muscle proteins and toxins, proteins and oncology and immune proteins and viral proteins, ~ 200 domestic and overseas participants

## 21st IUBMB and 12th FAOBMB International Congress of Biochemistry and Molecular Biology

August 2-7th, 2009

### Organizing Institutions

International Union of Biochemistry and Molecular Biology (IUBMB)
Federation of Asian and Oceanian Biochemists and Molecular Biologists (FAOBMB)
Chinese Society of Biochemistry and Molecular Biology
Chinese Society of Cell Biology
SIBCB

### Summary

36 sessions, 254 invited speakers (including 4 Nobel laureates) with topic covering genome dynamics and gene regulation, protein structure dynamics and proteomics, cell signaling and network and molecular basis of diseases, ~ 3,000 domestic and overseas participants



# International and Regional Partnerships

## Asia-Pacific International Molecular Biology Network (A-IMBN)

SIBCB is a founding member institute of the Asia-Pacific International Molecular Biology Network (A-IMBN). Within the A-IMBN framework, 6 member institutes namely SIBCB, Institute of Biochemistry and Molecular Biology, Taiwan University (IBMB), Institue of Medical Science, University of Tokyo (IMS), Institute for Virus Research, Kyoto Univeristy (IVR), Institute of Molecular Biology and Genetics, Seoul National University (IMBG) and Samsung Biomedical Research Institute, Sungkyunkwan University (SBRI) have been coorganizing the East Asia Joint Symposium on Biomedical Research (EAJSBR) since 2002. As an annual symposium held by turns among China, Japan and South Korea, EAJSBR has gradually developed into a successful platform to promote scientific discussion and collaboration among researchers from these 6 institutes and beyond.

## Cross-Strait Symposium on Biomedical Research

Since 2001, SIBCB and IBMB have been coorganizing the Cross-Strait Symposium on Biomedical Research (CSSBR). As an annual symposium held in Mainland and Taiwan by turns, CSSBR has gradually developed into a successful platform to promote understanding and collaboration among researchers across the Taiwan Strait.

# International and Regional Partnerships

## Other International and Regional Partners

Relevant laboratories in prestigious institutions such as National Institutes of Health, Argonne National Laboratory, University of Chicago, Yale University, Emory University and European Molecular Biology Laboratory have agreed to accept trainees from NCPS Shanghai, and training programs have been operating since 2010. Currently, several trainees who finished their programs have returned to SIBCB and participated in the construction of NFPS Shanghai.

In 2007, SIBCB signed an agreement on developing collaborative research projects in stem cell biology and functional genomics with the Hospital of Sick Children, the Department of Molecular Genetics and the Terrence Donnelly Center for Cellular & Biomolecular Research of University of Toronto. By 2011, the two parties have coorganized 3 mini-symposiums in China and Canada. In addition, SIBCB has been working on strengthening partnership with the Department of Cell Biology and the Yale Stem Cell Center of Yale Univeristy, and plans to organize the first mini-symposium in Shanghai at the end of 2012.

SIBCB has also established active partnerships with Medical Research Council (MRC), National Center for Scientific Research (CNRS), National Institute of Health and Medical Research (INSERM), Max Planck Society (MPG), Moscow State University and University of Hong Kong.



# Other International Activities

## WANG Yinglai Lectures

In 2011, SIBCB launched "WANG Yinglai Lectures" to honor the late Professor Yinglai Wang, one of the Institute's founding directors, and to promote high-end international academic exchange. A strict selection process was set up to identify and invite world renowned biologists who are leaders/pioneers in their fields to give talk to, and interact with researchers from SIBCB and other institutions in Shanghai.

Dr. Don Cleveland
(April 23rd, 2012)

Dr. Dieter Söll
(December 13th, 2011)

Dr. Gary Felsenfeld
(September 13th, 2011)

Dr. Elaine Fuchs
(October 28th, 2011)

## Editorial Board Members of International Journals

| | |
|---|---|
| The Journal of Biological Chemistry | Naihe Jing, Lin Li, Enduo Wang, Jiarui Wu |
| Molecular and Cellular Biology | Anning Lin, Xueliang Zhu, Jinqiu Zhou |
| MBoC Molecular Biology of the Cell | Gang Pei (Editor in Chief), Naihe Jing, Ming Lei, Lin Li, Yiping Li, Kan Liao, Anning Lin, Xiaolong Liu, Jiarui Wu, Yonglian Zhang, Xueliang Zhu |
| PLoS Genetics | Rong Zeng |
| Cell Research | Jianguo Song, Jiarui Wu, Xiaoyan Ding, Naihe Jing |
| MCP Molecular & Cellular Proteomics | Naihe Jing, Jiarui Wu |
| Molecular Cancer | Zhengjun Chen, Naihe Jing |
| BMC Systems Biology | Naihe Jing, Jianping Ding, Jiewen Zhou (James Chou) |
| BMC Developmental Biology | Naihe Jing, Hongyu Hu, Gang Wang |
| IUBMB Life | |
| Journal of Cellular Biochemistry | |
| Mechanisms of Development | |
| Developmental Dynamics | |
| BMC Structural Biology | |
| Gene Expression Patterns | |
| Protein & Peptide Letters | |
| Transcription | |

## Visits to/from SIBCB

From 2009 to 2011, 1,065 overseas scientists visited SIBCB, and 353 SIBCB scientists went abroad for academic purposes.

On April 9th, 2010, Dr. James Watson, winner of the 1962 Nobel Prize in Physiology or Medicine, visited SIBCB

On October 26th, 2011, Dr. Thomas A. Steitz and Dr. Venkatraman Ramakrishnan, winners of the 2009 Nobel Prize in Chemistry, visited SIBCB

# Graduate Education

Graduate Program

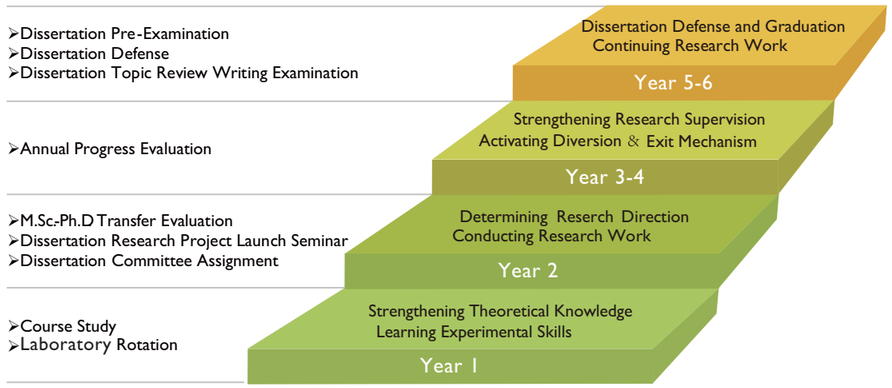
Graduate Students

## Graduate Program

SIBCB operates graduate programs in Biochemistry & Molecular Biology, Cell Biology and Developmental Biology. At the end of July 2012, SIBCB has an enrollment of 428 Ph.D. students.

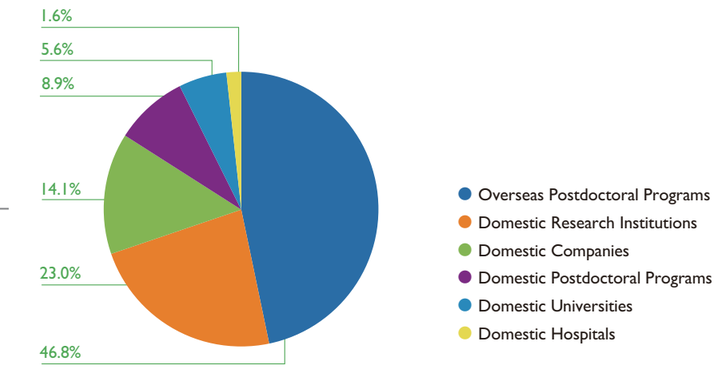
### Graduate Program

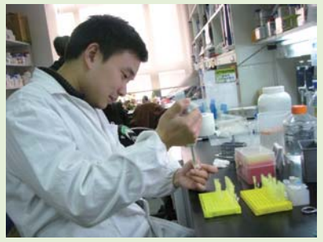
- A graduate program in line with counterparts in Western institutions including first-year laboratory rotation, qualification examinations and dissertation committee
- Multiple checkpoints to secure the quality of graduate training including M.Sc.-Ph.D. transfer evaluation, annual progress evaluation and diversion & exit mechanism
- A series of academic exchange platforms including domestic and international scientific meetings, SIBCB annual retreat, SLMB and SKLCB annual meetings, invited seminars, graduate academic salon and the First Author Forum




### Graduate Prospects

Alumni Analysis (2009-2011)





Graduate students doing their experiments

Graduate students attending the 6th Siqi Forum (June 17th, 2011)

Graduate students chatting with undergraduate students participating in the SIBS Summer Camp (July 18th-22nd, 2011)

Two SIBCB grduate students, Mr. Rui Yue and Mr. Liang Ge (the 3rd and 4th from the right side, the 2nd row), attending the 2010 Lindau Nobel Laureate Meeting (June 27th-July 2nd, 2010)

SIBCB mid-autumn festival carnival (September 14th, 2011)

Graduate student Ms. Jing Liao (the 3rd from the left side) participated in the 2010 Norvatis BioCamp in Norvatis' Swiss headquarters (September 6th, 2010)

SIBCB basketball team after winning the CAS Shanghai Branch basketball championship (June 12th, 2011)





## Graduate Student Awards and Honors (2009-2012)

| Award/Honor Name | Awardee (Supervisor) |
|---|---|
| Ray Wu Prize | 2012 Pengyu Huang (Lijian Hui), Hui Yang (Jinsong Li), Tianpeng Gu (Guoliang Xu)<br>2010 Rui Yue (Gang Pei)<br>2009 Li Ma (Xueliang Zhu) |
| National 100 Excellent Ph.D. Thesis Award | 2011 Xiaoming Wang (Xiaolong Liu)<br>2009 Yufeng Shi (Gang Pei) |
| CAS 50 Excellent Ph.D. Thesis Award | 2011 Li Ma (Xueliang Zhu)<br>2010 Bing Luan (Gang Pei), Xiaoming Wang (Xiaolong Liu), Jian Cao (Baoliang Song)<br>2009 Mude Shi (Bing Sun) |
| CAS President's Award (outstanding grade) | 2011 Pengyu Huang (Lijian Hui), Youdong Pan (Jianfeng Chen)<br>2010 Rui Yue (Gang Pei)<br>2009 Bing Luan (Gang Pei) |
| CAS President's Award (excellent grade) | 2011 Zhenfei Li (Lin Li), Jingjie Tang (Baoliang Song)<br>2010 Jialei Hu (Guoliang Xu), Jing Liao (Lei Xiao), Chang Liu (Gang Pei)<br>2009 Yang Xiang (Degui Chen), Feilong Meng (Jinqiu Zhou), Li Ma (Xueliang Zhu) |
| Di Ao Scholarship (first grade) | 2011 Minyun Zhou (Jianping Ding), Yijun Gao (Hongbin Ji)<br>2010 Minyun Zhou (Jianping Ding), Hexin Shi (Chen Wang)<br>2009 Zhenning Zhang (Lan Bao), Xiaolong Zhou (Enduo Wang) |
| Yuehua Zhuli Excellent Ph.D. Scholarship | 2011 Taotao Chen (Gang Pei), Yuan Zhang (Bing Sun)<br>2010 Yibo Wu (Rong Zeng)<br>2009 Min Yin (Jiawei Zhou) |
| BHP Billiton Scholarship | 2010 Rui Yue (Gang Pei)<br>2009 Liang Ge (Baoliang Song) |
| Pfizer Scholarship (special grade) | 2011 Bingfa Sun (Jianping Ding), Yanyan Zhang (Yun Zhao)<br>2010 Bo Zhou (Jinqiu Zhou), Xianchi Dong (Jianping Ding), Xianghua Piao (Ligang Wu) |

Blooming cherry trees on SIBCB Yueyang campus.