Chinese Biological Investigators Society

12th Biennial Conference
December 21–25, 2018
Kylin Villa Hotel, Shenzhen, China

Promote Life Sciences by Chinese Scientists Worldwide

Co-organized By

Chinese Biological Investigators Society (CBIS)
Southern University of Science and Technology (SUSTech)
Chinese Society for Cell Biology (CSCB)
http://cbisociety.org/
http://www.sustc.edu.cn/
http://www.cscb.org.cn/meeting/CBIS/

Welcome Message

On behalf of the Board of Directors, we welcome you to Shenzhen, China, for the 12th Biennial Conference of the Chinese Biological Investigators Society (CBIS, 华人生物学家协会). We have an outstanding program – prepared by the Program Committee with input from our members – that covers diverse topics in basic and translational research in life sciences as well as new technological developments. The program features 4 keynote speeches, 15 society (plenary) and special presentations, and 28 concurrent sessions. In addition, there will be 3 special forums to share and discuss insights in career development, biotechnology entrepreneurship, and publication policies.

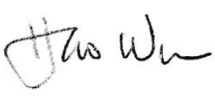
Our goal is to provide a unique platform for you to connect with scientists who share the same passion in life sciences as you do, to interact with industrial leaders who are experienced in bringing scientific findings from bench to bedside, and to explore new prospects for academic and industrial collaborations.

The CBIS, formally known as the Ray Wu Society, was established to honor Dr. Ray Wu's significant contributions in the advancement of Biochemistry and Plant Biotechnology, as well as his outstanding leadership in developing the Sino-America overseas student program known as CUSBEA. To extend Dr. Wu's legacy, we strive to promote scientific communications among Chinese scientists both internationally and in China. The Scientific Program consists not only the most prominent figures in the field but also outstanding investigators at all stages of their career.

We are particularly grateful this year for the financial support from the Southern University of Science and Technology China (SUSTech) and the opportunity to co-organize this meeting with SUSTech under President Shiyi Chen and the senior leadership, and with the Chinese Society for Cell Biology (CSCB) under the leadership of President Yeguang Chen. In addition, we are indebted to generous sponsorship from industry; the meeting will not be possible without it.

We hope that you will enjoy the hospitality of our local hosts and the interactions with colleagues as well as students from SUSTech and Shenzhen University. Shenzhen is a vibrant coastal city renowned for its modernization, its leading role in Chinese economy, and its proximity to other attractive cities including Guangzhou and Hong Kong. With spectacular science, natural beauty, and riches in culinary art, we are certain that both you and your family will fall in love.

We wish you all a memorable experience in Shenzhen.



Hao Wu (吴皓), Ph.D.
CBIS President

Guo-Min Li (李国民), Ph.D.
Program co-Chair 2018

Lei Li (李磊), Ph.D.
Program co-Chair 2018

Table of Contents

Meeting Program

Day 1, December 21, 2018, Friday, Arrival

12:00 pm – 10:00 pm Registration and election ballot distribution (Hotel Lobby)

6:00 – 6:05 pm Welcome address, Kylin Hall (麒麟厅)
Hao Wu, CBIS President, Harvard University

6:10- 7:10 pm CBIS Keynote Lecture
Chair: Zhenyu Yue, Mt Sinai Medical School

Yoshinori Ohsumi, Nobel Laureate, Tokyo Institute of Technology
"Lessons from Yeast – Autophagy as a Cellular Recycling System"

7:15 pm – 8:30 pm *Welcome Reception* – Wutong Hall/Fenghuang Hall (梧桐阁/凤凰阁)

Day 2, December 22, 2018, Saturday

8:45 – 9:10 am Conference Opening Ceremony, Kylin Hall (麒麟厅)

8:45 – 8:55 am Opening remarks by Hao Wu, CBIS President

8:55 – 9:10 am Opening remarks by 郭雨蓉, 南方科技大学党委书记

9:15–10:15 am CBIS Keynote Lecture
Session Chair: Guo-Min Li, UT Southwestern Medical Center

Bruce Beutler, Nobel Laureate. UT Southwestern Medical Center
"Solving new phenotypes induced by a germline mutagen in real time"

10:15 – 12:30 pm Society Lectures I, Kylin Hall (麒麟厅)
Chair: Yingzi Yang, Harvard University

10:15 – 10:45 am Xuetao Cao Nankai University
"Crosstalk of epigenetic modifiers and innate molecules in immunity and inflammation"

10:45 – 11:00 am *Break*

11:00 – 11:30 am CBIS Teaching Award presentation
Yibin Kang Princeton University

Liqun Luo Stanford University/HHMI
"Connections and communications between distributed neural circuits"

11:30 – 12:00 am Weimin Zhong Yale University
"Psychic Stem Cells and the Connection between Regeneration, Degeneration and Cancer"

12:00 – 12:30 pm Xi He Boston Children Hospital/HMS
"Wnt signaling in vertebrate development and stem cell biology"

12:30 – 2:00 pm *Lunch*, Wutong Hall/Fenghuang Hall (梧桐阁/凤凰阁)

2:00 – 4:00 pm Concurrent Sessions

1. Signaling in Diseases — Kylin Hall 1 (麒麟厅1)
2. Neural Circuit and Development — Kylin Hall 3 (麒麟厅3)
3. DNA and RNA Modification — Mumian Hall (木棉厅)
4. Metabolism and Cancer — Ziyun Hall (紫云阁)
5. Plant Biology — Dujuan Hall (杜鹃厅)
6. Chromatin Remodeling and 3D Genome — Zijing Hall (紫荆厅)
7. Late-Breaking Session — Longteng Hall (龙腾阁)

4:00 – 4:30 pm *Break*

4:30 – 6:30 pm Concurrent Sessions

8. Tumor immunology — Kylin Hall 1 (麒麟厅1)
9. Molecular and Cellular Mechanisms of Neurodegeneration — Kylin Hall 3 (麒麟厅3)
10. Chemical Biology — Longteng Hall (龙腾阁)
11. Cell Microenvironment and Diseases — Ziyun Hall (紫云阁)
12. Cancer Therapy — Zijing Hall (紫荆厅)
13. Abstract Session I — Dujuan Hall (杜鹃厅)
14. New Investigators Session I — Mumian Hall (木棉厅)

6:30 – 7:45 pm *Dinner,* Wutong Hall/Fenghuang Hall (梧桐阁/凤凰阁)

8:00 – 9:30 pm Panel Discussion I International conference hall (国际会议厅)
Entrepreneurship and Opportunities
Co-Chair Xiaodong Wang (王晓东, 北京生命科学研究所所长，百济神州创始人)
Charlene Liao (廖晓伶博士，Immune-Onc Therapeutics, Inc. 创始人, 总裁兼首席执行官)

Panelists:

- Steve Yang (杨青博士, 药明康德新药开发有限公司执行副总裁及首席商务官)
- Zhizhong Li (李治中博士, 又名菠萝，深圳拾玉儿童公益基金会联合创始人, 北京大学药学院客座教授, 科普公众号"菠萝因子"创始人/运营者)
- 尚立斌博士 (百济神州生物药业有限公司业务运营副总裁)
- Jacky Cao (曹德骏，罗氏诊断中国公司分子解决方案-生命科学和组织诊断部资深商务发展经理)

Day 3, December 23, 2018, Sunday

8:00 – 8:45 am CBIS Keynote Lecture, Kylin Hall (麒麟厅)
Session Chair: Hao Wu, Harvard University

Dinshaw Patel, Memorial Sloan Kettering Cancer Center
"Structural Biology of CRISPR-Cas Surveillance complexes"

8:45 – 11:00 am Society Lectures II, Kylin Hall (麒麟厅)
Session Chair: Yijun Qi, Tsinghua University

8:45 – 9:15 am Jiahuai Han Xiamen University
"Quantitative analysis of signaling pathways in inflammatory cell activation"

9:15 – 9:45 am Guoliang Xu SIBCB
"A vitamin C-derived DNA modification catalyzed by a TET-related oxidase mediates epigenetic regulation of photosynthesis"

9:45-10:00 am *Break*

10:00 – 10:30 am Ye-Guang Chen Tsinghua University
"Modulation of TGF-β signaling"

10:30 – 11:00 am Haifan Lin Yale University
"Piwi Proteins and piRNAs: A new paradigm in Gene Regulation"

11:00 – 12:10 pm CBIS Awards Presentation and Lectures, Kylin Hall (麒麟厅)

11:00 – 11:10 am Award Announcements
Session Chair: Yibin Kang, Princeton University
Award Presenting: Hao Wu, CBIS President, Harvard University

Ray Wu Award: Zhijian "James" Chen UT Southwestern Medical Center
Xinnian Dong Duke University

CBIS Teaching award:
Liqun Luo Stanford University

CBIS/《Science China – Life Science》Young Investigator Award:
Kun Zhang UC San Diego
Zhihua Liu Institute of Biophysics, CAS

11:10 – 11:40 pm Zhijian "James" Chen UT Southwestern Medical Center
"The cGAS-STING pathway of innate immunity"

11:40 – 12:10 pm Xinnian Dong Duke University
"Breaking the disease triangle with the circadian clock"

12:10 – 2:00 pm *Lunch,* Wutong Hall/Fenghuang Hall (梧桐阁/凤凰阁)

1:30 – 1:50 pm Dr. Letian Kuai WuXi App Tec/ZiYun Hall (紫云阁)
Unleashing DNA-Encoded Library Technology: Drug discovery and Beyond

2:00 – 4:00 pm Concurrent sessions

15. RNA-biology	Kylin Hall 1 (麒麟厅1)
16. Inflammation and Autoimmune Diseases	Kylin Hall 3 (麒麟厅3)
17. Stem Cells in Homeostasis and Injury Repair	Ziyun Hall (紫云阁)
18. Infection and Host Defense	Zijing Hall (紫荆厅)
19. Tumor Microenvironment and Metastasis	Dujuan Hall (杜鹃厅)
20. Epigenetic Regulation	Mumian Hall (木棉厅)
21. Genome Maintenance	Longteng Hall (龙腾阁)

4:00 – 4:30 *Break*

4:30 – 6:30 pm Concurrent sessions

22. Structural Biology	Kylin Hall 1 (麒麟厅1)
23. Protein and organelle homeostasis	Kylin Hall 3 (麒麟厅3)
24. Development and Human Diseases	Longteng Hall (龙腾阁)
25. Liver physiology and metabolic homeostasis	Dujuan Hall (杜鹃厅)
26. Systems Biology and Omics	Ziyun Hall (紫云阁)
27. New Investigators Session II	Zijing Hall (紫荆厅)
28. Abstract Session II	Caiyun Hall (彩云阁)

6:30 – 7:45 pm *Dinner,* Wutong Hall/Fenghuang Hall (梧桐阁/凤凰阁)

8:00 – 10:30 pm Panel discussions, International Conference Hall (国际会议厅)

8:00 – 9:00 pm Panel Discussion II – Academy Skills Development
Co-chairs: Kun-Liang Guan, University of California, San Diego
Junjie Chen, UT MD Anderson Cancer Center

Panelists:
Feng Shao, National Institute of Biological Sciences, Beijing
Guo-Liang Xu, Institute of Biochemistry and Cell Biology, CAS & Fudan University Medical School, Shanghai.

9:00 – 10:30 pm Panel Discussion III – Scientific Publication Policies and Strategies
Co-chairs: Xinnian Dong and Xiang-Dong Fu

Journal editor panelists:
Angela Eggleston, Senior Editor, Nature Press
Dangsheng Li, Editor-in-Chief, Cell Research

Day 4, December 24, 2018, Monday

8:00 –8:45 am CBIS Keynote Lecture, Kylin Hall (麒麟厅)
Session Chair: Lei Li, MD Anderson Cancer Center

Lieping Chen Yale University
"A paradigm shift in cancer immunotherapy: from enhancement to normalization"

8:45 – 11:45 am Society Lectures III, Kylin Hall (麒麟厅)
Session Chair: Lingling Chen, SIBCB, Chinese Academy of Sciences

8:45 – 9:15 am Xin Lu Oxford University Ludwig Inst.
"Cellular plasticity, cellular heterogeneity and single cell sequencing"

9:15 – 9:45 am Feng Shao NIBS
"Innate sensing of cytosolic LPS: pyroptosis and beyond"

9:45 – 10:15 am Junjie Chen MD Anderson
"Targeting DNA damage repair in cancer therapy"

10:15 – 10:45 am *Break*

10:45 – 11:15 am Lee Zou MGH, Harvard
"The ATR Signaling Circuitry: from Basic Research to Targeted Cancer Therapy"

11:15 – 11:45 am Hongtao Yu UT Southwestern Medical Center/HHMI
"Mitotic Checkpoint Regulators in Chromosome Segregation and Insulin Signaling"

11:45 – 7:00 pm Organized activities

7:00 – 10:00 pm Closing Banquet, Kylin Hall (麒麟厅)

- Announcement of board member election results
- Remarks from incoming CBIS President
- Introduction of elected board members

Day 5, December 25, 2018, Tuesday

Departure, Bon Voyage!

Concurrent Session Program

1: Signaling in Diseases, Kylin Hall 1/麒麟厅1 **12/22, 2-4pm**

Co-Chairs: **Kun-Liang Guan**, University of California, San Diego, kuguan@ucsd.edu
Xin-Hua Feng, Zhejiang University, xfeng@bcm.edu

2:00 – 2:20 PM
Xiaodong Chen, The University of Texas Health Science Center, Xiaodong.Cheng@uth.tmc.edu
"Exchange proteins directly activated by cAMP as major therapeutic targets"

2:20 – 2:40 PM
Xin-Hua Feng, Zhejiang University, xfeng@bcm.edu
"Loss of TGF-beta Cytostatic Signaling in Cancer"

2:40 – 3:00 PM
Kun-Liang Guan, University of California, San Diego, kuguan@ucsd.edu
"Regulation of the Hippo tumor suppressor pathway"

3:00 – 3:20 PM
Xuelian Luo, UT Southwestern Medical Center, xuelian.luo@utsouthwestern.edu
"The STRIPAK PP2A complex couples upstream inputs to control Hippo kinase activation"

3:20 – 3:40 PM
Cun-Yu Wang– University of California, Los Angeles; cwang@dentistry.ucla.edu
"Metabolic Control of Adult Stem Cell Fate and Bone-Fat Balance in Aging"

3:40 – 4:00 PM

2: Neural Circuit and Development, Kylin Hall 3/麒麟厅3 12/22, 2-4pm

Co-Chairs: **Liping Wang**, Shenzhen Institutes of Advanced Technology, CAS. brainresearch@qq.com
Hongwei Dong, University of Southern California, Hongwei.Dong@loni.usc.edu

2:00 – 2:20 PM
Yulong Li, School of Life Sciences, Peking University, yulongli@pku.edu.cn
"Identification of Human MRGPRX4 as A Novel Bile Acid Receptor for Chronic Itch"

2:20 – 2:40 PM
Xiangmin Xu, University of California, Irvine, xiangmin.xu@uci.edu
"New Hippocampal Circuit Organization and Function"

2:40 – 3:00 PM
Fuqiang Xu, Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences, fuqiqng.xu@wipm.ac.cn
"Virus-based tools for neurocircuit studies"

3:00 – 3:20 PM
Guoqiang Bi, University of Science and Technology of China, gqbi@ustc.edu.cn
"Multiscale imaging of neuronal synapses and circuits"

3:20 – 3:40 PM
Hongwei Dong, University of Southern California, Hongwei.Dong@loni.usc.edu
"Assembling global neural networks of the mouse brain"

3:40 – 4:00 PM
Tian Xue, University of Science and Technology of China, Hefei, xuetian@ustc.edu.cn
"**Intrinsic photosensitive retinal ganglion cells mediate light facilitated cross-modal cortical development**"

3: DNA and RNA Modification, Mumian Hall/木棉厅 **12/22, 2-4pm**

Co-Chairs: **Chuan He**, University of Chicago, chuanhe@uchicago.edu
Chengqi Yi, Peking University, chengqi.yi@pku.edu.cn

2:00 – 2:20 PM
Yungui Yang, Beijing Institute of Genomics, Chinese Academy of Sciences, ygyang@big.ac.cn
"Gene Regulations Mediated by RNA Modifications"

2:20 – 2:40 PM
Jianjun Chen, Beckman Research Institute of City of Hope, jianchen@coh.org
"The Role and Therapeutic Implication of RNA Modification in Cancer"

2:40 – 3:00 PM
Hongjun Song, Perelman School of Medicine, The University of Pennsylvania, shongjun@pennmedicine.upenn.edu
"Epitranscriptomic regulation in the mammalian nervous system"

3:00 – 3:20 PM
Linheng Li, Stowers Institute for Medical Research, LIL@stowers.org
"Expanding human blood-forming stem cells via manipulating the M6A pathway"

3:20 – 3:40 PM
Housheng Hansen He, Princess Margaret Cancer Center, University Health Network, hansenhe@uhnresearch.ca
"m^{6}A epitranscriptome profiling in patient tumors"

3:40 – 4:00 PM
Chengqi Yi, Peking University, chengqi.yi@pku.edu.cn
"Chemical-assisted sequencing of DNA and RNA modifications"

4: Metabolism and Cancer, Ziyun Pavilion/紫云阁 **12/22, 2-4pm**

Co-Chairs: **Zhimin Lu**, The University of Texas MD Anderson Cancer Center, zhiminlu@mdanderson.org
Baoliang Song, Wuhan University, blsong@whu.edu.cn

2:00 – 2:20 PM
Zhimin Lu, The University of Texas MD Anderson Cancer Center, zhiminlu@mdanderson.org
"Metabolic Feature of Cancer Cells"

2:20 – 2:40 PM
Baoliang Song, Wuhan University, blsong@whu.edu.cn
"Exploring the regulatory mechanism of cholesterol homeostasis"

2:40 – 3:00 PM
Wei Xu, University of Wisconsin, Madison, wxu@oncology.wisc.edu
"Central roles of PKM2 in the regulation of glucose and lipid metabolism"

3:00 – 3:20 PM
Yiguo Wang, School of Life Sciences, Tsinghua University, wangyiguo@biomed.tsinghua.edu.cn
"Hormonal regulation of hepatic glucose metabolism"

3:20 – 3:40 PM
Deliang Guo, Ohio State University, deliang.guo@osumc.edu
"Lipid metabolism reprogramming in malignancy, from *de novo* synthesis to storage"

3:40 – 4:00 PM
Wei Qi, Shanghai Tech University, qiwei@shanghaitech.edu.cn
"Targeting cancer epigenome through PRC2 inhibitor"

5: Plant Biology, Dujuan Hall/杜鹃厅 **12/22, 2-4pm**

Co-Chairs: **Xuehua Zhong**, University of Wisconsin, Madison, xuehua.zhong@wisc.edu
Aiwu Dong, Fudan University, aiwudong@fudan.edu.cn

2:00 – 2:15 PM
Xuemei Chen, University of California, Riverside, xuemeic@ucr.edu
"Biogenesis and activities of plant microRNAs - The "Where" and "How""

2:15 – 2:30 PM
Xiaofeng Cao, Institute of Genetics & Developmental Biology, Chinese Academy of Sciences, xfcao@genetics.ac.cn
"Mechanisms and functions of histone demethylases in Arabidopsis"

2:30 – 2:45 PM
Weicai Yang, Institute of Genetics & Developmental Biology, Chinese Academy of Sciences, wcyang@genetics.ac.cn
"Pollen tube guidance in flowering plants: The interplay between male and female gametophytes"

2:45 – 3:00 PM
Yinong Yang, Pennsylvania State University, yuy3@psu.edu
"Efficient gRNA expression and multiplex genome editing based on endogenous tRNA processing"

3:00 – 3:15 PM
Binglian Zheng, Fudan University, zhengbl@fudan.edu.cn
"Paternal miR159 triggers endosperm nuclear division by clearing maternal block in Arabidopsis"

3:15 – 3:30 PM
Hongwei Guo, Southern University of Science and Technology, guohw@sustc.edu.cn
"How Plant Smells: Signaling Mechanisms of Ethylene Gas"

3:30 – 3:45 PM
Dao-Xiu Zhou, Université Paris, dao-xiu.zhou@u-psud.fr
"Dynamics of rice epigenomes in plant development and adaptation to environment"

3:45 – 4:00 PM
Xuehua Zhong, University of Wisconsin, Madison, xuehua.zhong@wisc.edu
"Epigenetic switch regulating floral phase transition"

6: Chromatin Remodeling and 3D Genome, Zijing Hall/紫荆厅 12/22, 2-4pm

Co-Chairs: **Zhiguo Zhang**, Columbia University, zz2401@cumc.columbia.edu
Wei Xie, Tsinghua University, xiewei121@tsinghua.edu.cn

2:00 – 2:15 PM
Yijun Ruan, Jax Laboratory, Yijun.Ruan@jax.org
"Multiplexity in 3D genome organization and transcription regulation"

2:15 – 2:30 PM
Feng Yue, Penn State University, yuefeng.psu@gmail.com
"3D genome organization in cancer cells"

2:30 – 2:45 PM
Guohong Li, Institute of Biophysics, Chinese Academy of Sciences, liguohong@sun5.ibp.ac.cn
"Structure and dynamics of 30-nm chromatin fibers in gene regulation"

2:45 – 3:00 PM
Zhiguo Zhang, Columbia University, zz2401@cumc.columbia.edu
"DNA replication coupled nucleosome assembly in epigenetic inheritance and plasticity"

3:00 – 3:15 PM
Qing Li, Peking University, li.qing@pku.edu.cn
"Decode the communication between histone chaperones and replisome components"

3:15 – 3:30 PM
Geno Yujiang Shi, Harvard University, yujiang_shi@hms.harvard.edu
"Understanding the Epigenetic Basis Linking Pernicious Environment and Aging to Human Diseases"

3:30 – 3:45 PM
Yali Dou, University of Michigan, yalid@med.umich.edu
"MLL1 in development and diseases"

3:45 – 4:00 PM
Wei Xie, Tsinghua University, xiewei121@tsinghua.edu.cn
"Chromatin reprogramming during early animal development"

7: Late-Breaking Session, Longteng Parilion/龙腾阁 **12/22, 2-4pm**

Chair: **Xiao-Fan Wang**, Duke University Medical Center, xiao.fan.wang@duke.edu

2:00 – 2:20 PM
George Fu Gao, Institute of Microbiology, Chinese Academy of Sciences, gaof@im.ac.cn
"Medical Science Research and NSFC"

2:20 – 2:40 PM
Dihua Yu, The University of Texas MD Anderson Cancer Center, dyu@mdanderson.org
"Tumor Microenvironment-derived Exosomes (EVs) in Metastasis and Immune Activation"

2:40 – 3:00 PM
Chuan He, University of Chicago, chuanhe@uchicago.edu
"RNA methylation in translation regulation"

3:00 – 3:20 PM
Weijun Pan, Shanghai Institutes of Biological Sciences, Chinese Academy of Sciences, weijunpan@sibs.ac.cn
"Vcam-1+ Macrophages Guide Homing of Haematopoietic Stem and Progenitor Cells into a Vascular Niche"

3:20 – 3:40 PM
Qing Zhang, University of North Canolina School of Medicine, qing_zhang@med.unc.edu
"Studying Oxygen Sensing Pathway in Cancer"

3:40 – 4:00 PM
Dong Li, Institute of Biophysics, Chinese Academy of Sciences, lidong@ibp.ac.cn
"Visualizing intracellular organelle and cytoskeletal interactions with grazing incidence structured illumination microscopy"

8: Tumor immunology, Kylin Hall 1/麒麟厅1 **12/22, 4:30-6:30pm**

Co-Chairs: **Pan Zheng,** University of Maryland**,** PZheng@ihv.umaryland.edu
Chengchen (Alec) Zhang, UT Southwestern,
Alec.Zhang@UTSouthwestern.edu

4:30 – 5:00 PM
Di Yu, ANU College of Health and Medicine, di.yu@anu.edu.au
"Follicular cytotoxic T cells: localisation, transcriptional regulation and implication for cancer immunotherapy"

5:00 – 5:30 PM
Penghui Zhou, Sun Yat-sen University Cancer Center
"Identification of Cancer Immunotherapy Targets"

5:30 – 6:00 PM
Chengcheng (Alec) Zhang, UT Southwestern, Alec.Zhang@UTSouthwestern.edu
"Targeting ITIM-receptors for leukemia treatment"

6:00 – 6:30 PM
Pan Zheng, Institute of Human Virology, University of Maryland,
PZheng@ihv.umaryland.edu
"**Targeting host defense on DAMPs to prevent immunotherapy related adverse events**"

9: Molecular and Cellular Mechanisms of Neurodegeneration, Kylin Hall 3/麒麟厅3
12/22, 4:30-6:30pm

Co-Chairs: **Xiangdong William Yang**, David Geffen School of Medicine, University of California, Los Angeles, xwyang@mednet.ucla.edu
Xiao-Jiang Li, Emory University; Jinan University xli2@emory.edu

4:30 – 4:50 PM
Boxun Lu, School of Life Sciences, Fudan University, luboxun@fudan.edu.cn
"Allele-selective Degradation of Mutant HTT (mHTT) via Autophagy by mHTT-LC3 Linker Compounds"

4:50 – 5:10 PM
Zhenyu Yue, Icahn School of Medicine at Mount Sinai, zhenyu.yue@mssm.edu
"Regulation of □-Synuclein Transmission by Glial Autophagy in CNS"

5:10 – 5:30 PM
Xiangdong William Yang, David Geffen School of Medicine, University of California, Los Angeles, xwyang@mednet.ucla.edu
"Microglial Reprogramming to Ameliorate Pathological Phenotypes in Alzheimer's Disease"

5:30 – 5:50 PM
Junmin Peng, Center for Proteomics and Metabolomics, St. Jude Children's Research Hospital, Junmin.peng@stjude.org
"High Throughput Proteomics Approach to Understanding Alzheimer's Disease"

5:50 – 6:10 PM
Zhentao Zhang, Renmin Hospital of Wuhan University, zhentao104@gmail.com
"δ-secretase-cleaved Tau Stimulates Aβ Production via Upregulating STAT1-BACE1 signaling in Alzheimer's Disease"

6:10 – 6:30 PM
Xiao-Jiang Li, Emory University; Jinan University, xli2@emory.edu
"Genetically Modified Large Animal Models of Brain Diseases"

10: Chemical Biology, Longteng Parilion/龙腾阁 12/22, 4:30-6:30pm

Co-Chairs: **Yinsheng Wang**, University of California, Riverside, yinsheng.wang@ucr.edu
Fajun Nan, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, fjnan@simm.ac.cn

4:30 – 4:50 PM
Peng Chen, Peking University, pengchen@pku.edu.cn
"Bioorthogonal Cleavage Reactions in Space and Time: from Living Cells to Living Animals"

4:50 – 5:10 PM
Huiwang Ai, University of Virginia, huiwang.ai@virginia.edu
"A general strategy to red-shift green fluorescent protein based biosensors"

5:10 – 5:30 PM
Hang Hubert Yin, Tsinghua University, yin_hang@tsinghua.edu.cn
"Small Molecule Immunomodulators that Target Toll-Like Receptors"

5:30 – 5:50 PM
Xi Chen, University of California, Davis, xiichen@ucdavis.edu
"Chemoenzymatically synthesized carbohydrates as chemical biological probes and potential prebiotics"

5:50 – 6:10 PM
Yinsheng Wang, University of California Riverside, Yinsheng.wang@ucr.edu
"Quantitative proteomics for interrogating novel nucleic acid-binding proteins"

6:10 – 6:30 PM
Caiguang Yang, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, yangcg@simm.ac.cn
"Tackling untargeted protein in RNA epigenetics"

11: Cell Microenvironment and Diseases, Ziyun Pavilion/紫云阁,12/22, 4:30-6:30pm

Co-Chairs: **Guozhi Xiao**, Southern University of Science and Technology, xiaogz@sustc.edu.cn
Chuanyue Wu, Southern University of Science and Technology, wucy@sustc.edu.cn

4:30 – 5:00 PM
Chuanyue Wu, Southern University of Science and Technology, wucy@sustc.edu.cn
"Cell-extracelluar matrix adhesion: molecular basis, signaling and diseases"

5:00 – 5:30 PM
Weiguo Zhu, Shenzhen University, zhuweiguo@szu.edu.cn
"Histone modification and DNA damage repair"

5:30 – 6:00 PM
Guozhi Xiao, Southern University of Technology, xiaogz@sustc.edu.cn
"Osteocytic Kindlin-2 signaling modulates bone marrow microenvironment to regulate bone remodeling"

6:00 – 6:30 PM
Yi Sun, ZheJiang University, yisun@zju.edu.cn
The FBXW2-Catenin-MMPs axis regulates tumor invasion and metastasis

12: Cancer Therapy, Zijing Hall/紫荆厅 **12/22, 4:30-6:30pm**

Co-Chairs: **Xinyuan Fu**, Southern University of Science and Technology, fuxy@sustc.edu.cn
Hongjian Zhu, The University of Melbourne, hongjian@unimelb.edu.au

4:30 – 4:50 PM
Chenghua Yang, CAS Key Laboratory of Tissue Microenvironment and Tumor, Shanghai Institute of Nutrition and Health, Shanghai Institutes for Biological Sciences, University of Chinese Academy of Sciences, Chinese Academy of Sciences. chyang@sibs.ac.cn
"Development of Bcl10 peptide inhibitors for the treatment of ABC-DLBCL"

4:50 – 5:10 PM
Zhijie Chang, Tsinghua University, zhijiec@tsinghua.edu.cn
"Regulation of cell proliferation by a novel family protein p15RS and CREPT"

5:10 – 5:30 PM
Zhang Jian, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China
Jian.zhang@sjtu.edu.cn
"First-in-class Drug Design and Discovery"

5:30 – 5:50 PM
Quan Zhao, The State Key Laboratory of Pharmaceutical Biotechnology, School of Life Sciences, Nanjing University, Nanjing, China.
"Roles of NatD-mediated N-alpha-terminal acetylation of histone H4 in cancer metastasis"

5:50 – 6:10 PM
Hong-Jian Zhu, *The University of Melbourne, Melbourne*
"Exosomes and TGF-beta in Cancer: Biomarkers, Metastasis and Therapeutics"

6:10 – 6:30 PM
Xin-Yuan Fu, SUSTECH, NUS and West China Hospital
"The JAK-STAT Pathway to PeriGenetics and Clinical Applications"

13: Abstract Session I, Dujuan Hall/杜鹃厅 **12/22, 4:30-6:30pm**

Chair: **Zhenyu Yue**, Icahn School of Medicine at Mount Sinai, zhenyu.yue@mssm.edu

4:30 – 4:45 PM
Jun Sun, University of Illinois at Chicago, junsun7@uic.edu
"Vitamin D receptor is required to protect from tumorigenesis and dysbiosis via the JAK/STAT pathway"

4:45 – 5:00 PM
Jiahong Lu, Institute of Chinese Medical Sciences, University of Macau, jiahonglu@umac.mo
"Enhancing apoptotic cell clearance for inflammatory bowel disease intervention: a lesson from NRBF2 deficient mice"

5:00 – 5:15 PM
Fei Li, New York University, fl43@nyu.edu
"Heterochromatin regulate centromeres by protecting CENP-A from ubiquitin-mediated degradation"

5:15 – 5:30 PM
Zhihua Wang, Wuhan University Renmin Hospital, zhihuawang@whu.edu.cn
"Increased transcription and translation rates in cardiac hypertrophy are regulated by lncRNAs"

5:30 – 5:45 PM
Chunyu Wang, Rensselaer Polytechnic Institute, wangc5@rpi.edu
"NMR Structural Studies of Transmembrane Domain of APP"

5:45 – 6:00
Zhong-Wei Zhou, Sun Yat-sen University, Zhouzhw6@mail.sysu.edu.cn
NBS1 Cooperates with NOTCH Pathway in Neural Development

6:00 – 6:20 PM
Richard Lu, Cincinnati Children's Hospital Medical Center, Richard.Lu@cchmc.org
"Convergence of gliogenesis and brain tumorigensis at a single-cell level"

14: New Investigators Session I, Mumian Hall/木棉厅 12/22, 4:30-6:30pm

Chair: **Xin Sun**, University of California, San Diego, xinsun@ucsd.edu

4:30 – 4:50 PM
Xu Li, School of Life Science, Westlake University, lixu@westlake.edu.cn
"Deciphering the Disease-Related Signaling Pathways Using Functional Proteomics"

4:50 – 5:10 PM
Feng Li, Wuhan University College of Medicine, fli222@whu.edu.cn
"The role of histone demethylase in cancer"

5:10 – 5:30 PM
Weibo Luo, UT Southwestern, Weibo.Luo@UTSouthwestern.edu
"Epigenetic regulation of hypoxia responses in human cancers"

5:30 – 5:50 PM
Wenfei Jin, Southern University of Science and Technology, jinwf@sustc.edu.cn
"Comprehensive Mapping of Human Hematopoiesis and Leukemogenesis at Single Cell Resolution"

5:50 – 6:10 PM
Bo Li, UT Southwestern, Bo.Li@UTSouthwestern.edu
"Uncovering the landscape of tumor antigen-specific T cells"

6:10 – 6:30 PM
Youdong (Jack) Mao, School of Physics and Center for Quantitative Biology, Peking University, ymao@pku.edu.cn
"A dynamic view on the design principle of human 26S proteasome machinery"

15: RNA-biology, Kylin Hall 1/麒麟厅1 **12/23, 2-4pm**

Co-Chairs: Zefeng Wang, University of North Carolina at Chapel Hill, wangzefeng@picb.ac.cn
Xiangdong Fu, University of California, San Diego, xdfu@ucsd.edu

2:00 – 2:20 PM
Wei Chen, SUSTech Academy for Advance and Interdisciplinary Studies, chenw@sustc.edu.cn
"Systematic analysis on *cis*-regulatory code of polyadenylation"

2:20 – 2:40 PM
Yi Xing, University of Pennsylvania School of Medicine, yi.xing@pennmedicine.upenn.edu
"Elucidating alternative isoform variation using massive RNA-seq. data"

2:40 – 3:00 PM
Xiaohua Shen, Tsinghua University, xshen@tsinghua.edu.cn
"Novel functions of RNA-binding proteins in transcription regulation and stem cell pluripotency"

3:00 – 3:20 PM
Zhao Zhang, Carnegie Institution for Science, zzhang@carnegiescience.edu
"Why piRNAs are needed"

3:20 – 3:40 PM
Yang Yu, Institute of Biophysics, Chinese Academy of Sciences, yuyang@ibp.ac.cn
"A Pandas complex adapted for piRNA-guided transposon silencing"

3:40 – 4:00 PM
Mofang Liu, Shanghai Institute for Biochemistry and Cell Biology, Chinese Academy of Sciences, mfliu@sibcb.ac.cn
"A Novel Function of LARP7 in Regulating the 2′-O-methylation of U6 snRNA during Spermatogenesis in Mice"

16: Inflammation and Autoimmune Diseases, Kylin Hall 3/麒麟厅3 12/23, 2-4pm

Co-Chairs: **Yang Liu,** University of Maryland, YaLiu@ihv.umaryland.edu
Wu Li, Tsinghua University, wuli@mail.tsinghua.edu.cn

2:00 – 2:30 PM
Yang Liu, School of Medicine, University of Maryland Baltimore, yaliu@ihv.umaryland.edu
"CD24 and self-nonself discrimination: fundamental concept and translation"

2:30 – 3:00 PM
Zeng Wenwen. School of Life Science, Tsinghua University, wenwenzeng@tsinghua.edu.cn
"Neural regulation of white adipose tissue plasticity"

3:00 – 3:30 PM
Li Wu, Tsinghua University School of Medicine, wuli@tsinghua.edu.cn
"Dendritic cells and macrophages in Immune homeostasis"

3:30 – 4:00 PM
Bin Li, Shanghai Institute of Immunology, Shanghai Jiaotong University
binli@shsmu.edu.cn
"FOXP3+Treg functional stability and their clinical application"

17: Stem Cells in Homeostasis and Injury Repair, Ziyun Pavilion/紫云阁

12/23, 2-4pm

Co-Chairs: **Linheng Li**, Stowers Institute for Medical Research, LIL@stowers.org
Duangqing Pei, Guangzhou Institute of Biomedicine and Health, Chinese Academy of Sciences, pei_duanqing@gibh.ac.cn

2:00 – 2:20 PM
Qi Zhou, Institute of Zoology Chinese Academy of Sciences, gzhou@ioz.ac.cn
"Progress of stem cell research and translational application in China"

2:20 – 2:40 PM
Hongkui Deng, College of Life Sciences and Peking-Tsinghua Center for Life Sciences, hongkui_deng@pku.edu.cn
"Small molecules induced cell reprogram"

2:40 – 3:00 PM
Xiaoqun Wang, Institute of Biophysics, CAS, wangxiaochen@ibp.ac.cn
"Neural stem cell subtypes and cortical development"

3:00 – 3:20 PM
Zhenguo Wu, the Hong Kong University of Science and Technology, bczgwu@ust.hk
"Regulation of quiescence exit in muscle stem cells"

3:20 – 3:40 PM
Jingsong Li, Institute of Biochemistry and Cell Biology, CAS, jsli@sibcb.ac.cn
"Artificial sperm mediated gene editing"

3:40 – 4:00 PM
Daunqing Pei, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, pei_duanqing@gibh.ac.cn
"Single-cell analysis of three reprogramming systems reveals a generic model for cell fate transitions"

18: Infection and Host Defense, Zijing Hall/紫荆厅 **12/23, 2-4pm**

Co-Chair: **Bing Su,** Shanghai Jiao Tong University, bingsu@sjtu.edu.cn
Feng Shao, National Institute of Biological Sciences, shaofeng@nibs.ac.cn

2:00 – 2:20 PM
Xing Chang, Shanghai Institutes of Biological Sciences, Chinese Academy of Sciences changxing@sibs.ac.cn
"Regulation and manipulation of RNA processing in the immune system"

2:20 – 2:40 PM
Shan-Lu Liu, The Ohio State University, liu.6244@osu.edu
"Restriction of HIV infection by TIMs and viral antagonism lentivirus Nef"

2:40 – 3:00 PM
Qi-Jing Li, Duke University School of Medicine Qi-Jing.Li@Duke.edu
"Tumor as a Suppressive Immune Organ"

3:00 – 3:20 PM
Yisong Wan, The University of North Carolina at Chapel Hill, wany@email.unc.edu
"The control of helper T cell generation and function in inflammation and disease"

3:20 – 3:40 PM
Qiming Liang, Shanghai Institute of Immunology, lianggiming@shsmu.edu.cn
"Virus-host interactome reveals the unique blockage of host RNAi machinery by Zika virus"

3:40 – 4:00 PM
Jixi Li, State Key Laboratory of Genetic Engineering, lijixi@fudan.edu.cn
"Structural basis of cell necrosis and its implications in neurodegenerative diseases"

19: Tumor Microenvironment and Metastasis, Dujuan Hall/杜鹃厅 **12/23, 2-4pm**

Co-chairs: **Jing Yang, University of California, San Diego,** jiyang@ucsd.edu
Guohong Hu, Shang Institute for Biological Sciences, CAS ghhu@sibs.ac.cn

2:00 – 2:20 PM
Erwei Song, Sun Yat-sen University, songew@mail.sysu.edu.cn
"Treat the soil of tumor: turning foes into friends"

2:20 – 2:40 PM
Li Ma, The University of Texas MD Anderson Cancer Center, lma4@mdanderson.org
"A lncRNA saga in metastasis"

2:40 – 3:00 PM
Bin Zhou, Shanghai Institutes for Biological Sciences, zhoubin@sibs.ac.cn
"Fate mapping of epithelial-to-mesenchymal transition for tumor metastasis"

3:00 – 3:20 PM
Jing Yang, **University of California, San Diego**
"Epithelial-Mesenchymal Plasticity in Carcinoma Metastasis"

3:20 – 3:40 PM
Guohong Hu, Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences, ghhu@sibs.ac.cn
"Regulation of breast cancer metastasis organotropism"

20: Epigenetic Regulation, Mumian Hall/木棉厅 12/23, 2-4pm

Co-Chairs: **Haitao Li**, Tsinghua University, lht@tsinghua.edu.cn
Bing Li, Shanghai Jiao Tong University School of Medicine, bingli@shsmu.edu.cn

2:00 – 2:20 PM
Cheng-Ming Chiang, UT Southwestern, heng-ming.chiang@utsouthwestern.edu
"BRD4 in Transcription Programming and Cancer Therapy"

2:20 – 2:40 PM
Gang Wang, Shanghai Institutes of Biological Sciences, Chinese Academy of Sciences, gwang@sibcb.ac.cn
"Mediator-ing transcription and epigenetics in liver diseases"

2:40 – 3:00 PM
Bing Li, Shanghai Jiao Tong University, bingli@shsmu.edu.cn
"A Y-fork DNA binding protein coordinates histone nuclear shuffling and replication-coupled chromatin deposition"

3:00 – 3:20 PM
Yanming Wang, School of Life Sciences, Henan University, yuw12@psu.edu
"Histone hypercitrullination in autoimmunity and cancer metastasis"

3:20 – 3:40 PM
Xiaoling Li, National Institute of Environmental Health Sciences, lix3@niehs.nih.gov
"Metabolic and Epigenetic Regulation of Embryonic Stem Cell Maintenance and Differentiation"

3:40 – 4:00 PM
Haitao Li, Tsinghua University, lht@tsinghua.edu.cn
"Hierarchical Histone Deacetylation by Sirtuins"

21: Genome Maintenance, Longteng Parilion/龙腾阁 **12/23, 2-4pm**

Co-Chairs: **Zhiyuan Shen**, Rutgers Cancer Institute of New Jersey, shenzh@cinj.rutgers.edu
Daochun Kong, Peking University, kongdc@pku.edu.cn

2:00 – 2:20 PM
Zhenkun Lou, Mayo Clinic, lou.zhenkun@mayo.edu
"Regulation of DNA-Protein Crosslinks"

2:20 – 2:40 PM
Junran Zhang,The Ohio State University, Junran.Zhang@osumc.edu
"Identifying New Biomarkers to Guide the Use of Cell Cycle Checkpoint Inhibitors"

2:40 – 3:00 PM
Zhongsheng You, Washington University School of Medicine, zyou@wustl.edu
"Genome maintenance: signaling through Ca2+"

3:00 – 3:20 PM
Xingzhi Xu, Shenzhen University, xingzhi.xu@szu.edu.cn
"**MRN UFMylation promotes ATM activation"**

3:20 – 3:40 PM
Weihang Chai, Washington State University School of Medicine, wchai@wsu.edu
"Regulation of replication fork stability by ssDNA-binding proteins"

3:40 – 4:00 PM
Zhiyuan Shen, Rutgers Cancer Institute of New Jersey, Rutgers University, shenzh@cinj.rutgers.edu
"Genomic signatures of tumors initiated by BCCIP deficiency"

22: Structural Biology, Kylin Hall 1/麒麟厅1 **12/23, 4:30-6:30pm**

Co-Chairs: **Hongwei Wang**, Tsinghua University, hongweiwang@tsinghua.edu.cn
Ning Zheng, University of Washington, nzheng@uw.edu

4:30 – 4:50 PM
Xuewu Zhang, University of Texas Southwestern Medical Center, Dallas, Xuewu.Zhang@UTSouthwestern.edu
"Transmembrane signaling mechanisms of plexin"

4:50 – 5:10 PM
Weikai Li, Washington University at St. Louis, weikai@wustl.edu
"Structure basis of anticoagulation with vitamin K antagonization"

5:10 – 5:30 PM
Xinzheng Zhang, Institute of Biophysics - Chinese Academy of Sciences, xzzhang@ibp.ac.cn
"Near-atomic structure of PBCV-1, a nucleo-cytoplasmic large dsDNA virus"

5:30 – 5:50 PM
Beili Wu, Shanghai Institute of Materia Medica - Chinese Academy of Sciences, beiliwu@simm.ac.cn
"Structural basis of signal recognition and regulation at the full-length glucagon receptor"

5:50 – 6:10 PM
Hongwei Wang, Tsinghua University; hongweiwang@tsinghua.edu.cn
"How small a protein can be solved at high resolution by single particle cryo-EM?"

6:10 – 6:30 PM
Ning Zheng, University of Washington, nzheng@uw.edu
"The inner workings of the COMPASS H3K4 methyltransferase complex"

23: Protein and organelle homeostasis, Kylin Hall 1/麒麟厅3 12/23, 4:30-6:30pm

Co-Chairs: **Qing Zhong**, Shanghai Jiao Tong University School of Medicine, qingzhong@shsmu.edu.cn
Wei-Xing Zong, Ernest Mario School of Pharmacy, Rutgers University, zongwx@pharmacy.rutgers.edu

4:30 – 4:50 PM
Weixing Zong, Ernest Mario School of Pharmacy, Rutgers University, zongwx@pharmacy.rutgers.edu
"PI3 kinases in intracellular membrane trafficking"

4:50 – 5:10 PM
Quan Chen, The State Key Laboratory of Membrane Biology, Chinese Academy of Sciences, chenq@ioz.ac.cn
"Molecular regulation of selective mitophagy and its role in inflammasome activation and hepatocarcinogenesis"

5:10 – 5:30 PM
Anbing Shi, Tongji Medical College, Huazhong University of Science and Technology, ashi@hust.edu.cn
"Worming Our Way Through the Endosomal System"

5:30 – 5:50 PM
Qing Zhong, Shanghai Jiao Tong University School of Medicine, qingzhong@shsmu.edu.cn
"Biochemical Dissection and Reconstitution of Mammalian Autophagy"

5:50 – 6:10 PM
Yonghao Yu, UT Southwestern Medical Center at Dallas, Yonghao.Yu@UTSouthwestern.edu
"Navigating downstream of mTORC1: A Quantitative Phosphoproteomic Approach"

6:10 – 6:30 PM
Liangyi Chen, Institute of Molecular Medicine, Peking University, lychen@pku.edu.cn
"Fast, long-term super-resolution imaging with Hessian structured illumination microscopy and its application in clinical samples"

24: Development and Human Diseases, Longteng Parilion/龙腾阁,12/23, 4:30-6:30pm

Co-Chairs: **Lijian Hui**, Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, ljhui@sibcb.ac.cn
Nan Tang, National Institute of Biological Sciences, Beijing, tangnan@nibs.ac.cn

4:30 – 4:50 PM
Xin Sun, University of California, San Diego, xinsun@ucsd.edu
"Consider the Lung as a Sensory Organ"

4:50 – 5:10 PM
Yi Arial Zeng, Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, yzeng@sibcb.ac.cn
"Protein C Receptor In Regulating Mammary Stem Cells And Breast Cancer"

5:10 – 5:30 PM
Ting Chen, National Institute of Biological Sciences, Beijing chenting@nibs.ac.cn
Mesenchymal niche heterogeneity and plasticity"

5:30 – 5:42 PM
Ji-Feng Fei, Institute of Brain Research and Rehabilitation, South China Normal University, jifengfei@m.scnu.edu.cn
"Axolotl, an ideal model for dissecting the mystery of spinal cord regeneration"

5:42 – 5:54 PM
Pengyu Huang, School of Life Science and Technology, Shanghai Tech University, huangpy@shanghaitech.edu.cn
"Regulation of liver regeneration during chronic liver injuries"

5:54 – 6:06 PM
Dali Li, East China Normal University, dlli@bio.ecnu.edu.cn
"Genome editing for diseases modeling and gene therapy"

6:06 – 6:18 PM
Yan Song, School of Life Sciences, Peking University, yan.song@pku.edu.cn
"Commitment matters: Timely and robust cell fate commitment in neural stem cell lineages"

6:18 – 6:30 PM
Bo Zhou, Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, bo.zhou@sibcb.ac.cn
"When hematopoietic stem cells meet puberty"

25: Liver physiology and metabolic homeostasis, Dujuan Hall/杜鹃厅

12/23, 4:30-6:30pm

Co-Chairs: **Xiao-bo Zhong**, University of Connecticut, xiaobo.zhong@uconn.edu
Huichang Bi, Sun Yat-Sen University, bihchang@mail.sysu.edu.cn

4:30 – 4:45 PM
Xiao-bo Zhong, University of Connecticut, xiaobo.zhong@uconn.edu
"Control of postnatal liver maturation by nuclear receptors and lncRNAs"

4:45 – 5:00 PM
Wen Xie, University of Pittsburgh, wex6@pitt.edu
"Disease effect on liver metabolism"

5:00 – 5:15 PM
Chaohui Yu, Zhejiang University, ych623@sina.com
"Vitamin D receptor (VDR) and non-alcoholic fatty liver disease (NAFLD)"

5:15 – 5:30 PM
Wendong Huang, Beckman Research Institute of City of Hope, whuang@coh.org
"Bile acid receptors in regulating fatty liver diseases"

5:30 – 5:45 PM
Shi-mei Zhuang, Sun Yat-Sen University, lsszsm@mail.sysu.edu.cn
"Vessels that encapsulate tumor clusters (VETC) in HCC metastasis and therapeutic response"

5:45 – 6:00 PM
Ai-ming Yu, University of California at Davis, aimyu@ucdavis.edu
"ncRNAs in the control of liver metabolism and hepatocellular carcinoma (HCC)"

6:00 – 6:15 PM
Huichang Bi, Sun Yat-Sen University, bihchang@mail.sysu.edu.cn
"Pregnane X receptor in hepatomegaly and liver regeneration"

26: Systems Biology and Omics, Ziyun Pavilion/紫云阁 12/23, 4:30-6:30pm

Co-Chairs: **Kun Zhang**, University of California, San Diego, kzhang@bioeng.ucsd.edu
Li Yang, MPG Partner Institute for Computational Biology, Chinese Academy of Sciences, liyang@picb.ac.cn

4:30 – 4:50 PM
Sheng Zhong, University of California, San Diego, szhong@eng.ucsd.edu
"Rainbow-seq: combining cell lineage tracing with single-cell RNA sequencing in preimplantation embryos"

4:50 – 5:10 PM
Xiu-Jie Wang, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, xjwang@genetics.ac.cn
"m^{6}A RNA modification: mechanism, function and social implications"

5:10 – 5:30 PM
Bin Zhang, Icahn School of Medicine at Mount Sinai, bin.zhang@mssm.edu
"Network Modeling of Large-scale Multi-Omics Data Reveals Novel Pathways and Key Regulators in Alzheimer's Disease"

5:30 – 5:50 PM
Yong Zhang, School of Life Science and Technology, Tongji University, yzhang@tongji.edu.cn
"Inherited epigenetic signatures prime the establishment of zygotic transcriptional regulation during early embryogenesis"

5:50 – 6:10 PM
Li Yang, MPG Partner Institute for Computational Biology, Chinese Academy of Science, liyang@picb.ac.cn
"Harness unintended nucleic acid mutation to targeted base editing"

6:10 – 6:30 PM
Kun Zhang –University of California, San Diego, kzhang@bioeng.ucsd.edu
"Integrative single-cell analysis by transcriptional and chromatin states of the brain"

27: New Investigators Session II, Zijing Hall/紫荆厅 12/23, 4:30-6:30pm

Chair: **Ling-Ling Chen,** Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Science, linglingchen@sibcb.ac.cn

4:30 – 4:50 PM
Liang Chen, Wuhan University, Liang_chen@whu.edu.cn
"R-loop: a Unique Nucleic Acid Structure in Relation to Transcription Regulation and Disease"

4:50 – 5:10 PM
Pu Gao, Institute of Biophysics, Chinese Academy of Science, gaopu@ibp.ac.cn
"Host-Pathogen Interaction: Pathogen-Mediated Non-Canonical Ubiquitination"

5:10 – 5:30 PM
Jiazhi Hu, Peking University, hujz@pku.edu.cn
"Studying genome stability during genome editing by primer-extension sequencing"

5:30 – 5:50 PM
Sheng Wang, Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Science, wangsheng@sibcb.ac.cn
"Structure-Based Ligand Discovery Against Dopamine Receptor"

5:50 – 6:10 PM
Hui Yang, Institute of Biochemistry and Cell Biology, Chinese Academy of Science, yanghui@sibcb.ac.cn
"Recognition mechanism and inhibition of DNA targeting by CRISPR-Cas systems"

6:10 – 6:30 PM
Di Zhao, The University of Texas MD Anderson Cancer Center, DZhao2@mdanderson.org
"Synthetic essentiality of chromatin remodeling factor CHD1 in PTEN deficient cancer"

28: Abstract Session II, Caiyun Pavilion/彩云阁 12/23, 4:30-6:30pm

Chair: **Jingwu Xie**, Indiana University School of Medicine, jinxie@iu.edu

4:30 – 4:50 PM
Jingwu Xie, Indiana University School of Medicine, jinxie@iu.edu
"Drug resistance in gastric and pancreatic cancer"

4:50 – 5:10 PM
Xuefeng Chen, College of Life Sciences, Wuhan University, xfchen@whu.edu.cn
"Bre1-dependent H2B ubiquitination promotes homologous recombination by stimulating histone eviction at DNA breaks"

5:10 – 5:30 PM
Min Dong, Boston Children's Hospital, Harvard Medical School,
min_dong@hms.harvard.edu
"Turning bacterial toxins into therapeutics – developing a toxin-derived Wnt signaling inhibitor"

5:30 – 5:50 PM
Jian Lu, Peking University**,** luj@pku.edu.cn
"Decreased Biosynthetic Energy Cost for Amino Acids in Cancer Evolution"

5:50 – 6:10 PM
Yan Yan, Hong Kong University of Science and Technology, yany@ust.hk
"The Drosophila scribble mutant cells display evolving properties during tumor progression"

6:10 – 6:30 PM
Ping Ao, Shanghai Jiaotong University, aoping@sjtu.edu.cn
Systems Biology Approach: endogenous network theory for normal and abnormal developmental dynamical processes"

Keynote, Plenary Session, & Panel Speakers

Yoshinori Ohsumi, PhD
Honorary Professor
Frontier Research Center
Tokyo Institute ofTechnology, Tokyo, Japan

Education
- The University of Tokyo,
  College of Art s and Sciences, B. Sc. 1967
  Graduate School of Sciences, M .Sc. 1969
  Graduate School of Sciences, D.Sc. 1974

Research Interests
- Cell biologist specializing in autophagy

Major Awards
- Thom son Reuters Citation Laureates 2013
  Canada Gairdner International Award 2015
  International Prize for Biology 2015
  The Lewis S. Rosenst iel Award 2016
  The Wiley Prize 2016
- The Dr. Paul Jans sen Award 2016
  Breakthrough Prize in Life Sciences 2016
- The Nobel Prize in Physiology or Medicine 2016

Experience
1974-1977:Post Doctoral Fellow, Rockefeller University
1977-1986:Research Associate, Department of Biology, Faculty of Science, The University of Tokyo
1986-1988:Lecturer, Department of Biology, Faculty of Science, The University of Tokyo
1988-1996:Associate Professor, Depar tment of Biology, College of Arts and Sciences, The University of Tokyo
1996-2009:Professor, Department of Cell Biology, National Insti tute for Basic Biology, Okazaki Prof essor, The Graduate University for Advanced Studies
2009-2014: Professor , Advanced Research Organization, Frontier Research Center, Tokyo Institute of Technology
2014-present : Honorary Professor , Frontier Research Center, Tokyo Institute of Technology

Lessons from Yeast – Autophagy as a Cellular Recycling System

Every cellular event is achieved through a balance between synthesis and degradation. The cellular degradation process is highly regulated and plays critical roles in cell physiology. Thirty years ago I first found under a light microscope that the yeast S. cerevisiae induces massive protein degradation within the vacuole under nutrient starvation. Electron microscopy revealed that membrane dynamics during this process are topologically identical with known autophagy in mammals. Taking advantage of the yeast system, many autophagy-defective mutants were successfully obtained. Now we know that 18 ATG genes are essential for starvation-induced autophagy. These Atg proteins concertedly function in the formation of autophagosome, sequestration process of cytoplasmic constituents. Soon we uncovered that most ATG genes are conserved from yeast to mammals and plants. The identification of ATG genes had completely changed the landscape of autophagy research. Genetic manipulation of the ATG genes unveiled a really broad range of physiological functions of autophagy. Autophagy plays critical roles not only in nutrient recycling, but also intracellular clearance through the elimination of harmful proteins and damaged organelles. It is becoming clear that autophagy is relevant to many diseases and has become one of the most popular field in cell biology. However, my group have been working on the yeast Atg proteins to understand the mechanisms of the unique membrane dynamics during autophagy. We also found that autophagy plays important roles in the homeostasis of certain ions, moreover, not only proteins but also RNA is degraded via autophagy. Now we are trying to elucidate degradation of cytoplasmic proteins under various conditions more quantitatively.

大竹明美

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科学技術創成研究院　細胞制御工学研究センター
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大隅基礎科学創成財団　http://www.ofsf.or.jp/

Bruce Beutler, M.D.
Regental Professor and Director
Center for the Genetics of Host Defense,
UT Southwestern Medical Center
Dallas, Texas U.S.A.

Education

- The University of California, San Diego, CA
  Revelle College, B. A. 1976
- The University of Chicago, Chicago, IL
  M. D. 1981

Research Statement

My research goals are to advance the fundamental understanding of the Genetics of immunity, to aid in the treatment of infection, cancer, and autoimmunity.

Major Awards

- Robert Koch Prize 2004
- William B. Coley Award 2006
- Gran Prix Charles-Leopold Mayer 2006
- Balzan Prize 2007
- Frederik B. Bang Award 2008
- Will Rogers Institute Annual Prize for Scientific Research 2009
- Albany Medical Center Prize in Medicine and Biomedical Research 2009
- Shaw Prize 2011
- Nobel Prize in Physiology or Medicine 2011

Experience

- 1981-1982: Intern, Department of Medicine, UT Southwestern Medical Center, Dallas, TX
- 1982-1983: Resident, Department of Neurology, UT Southwestern Medical Center, Dallas, TX
- 1983-1985: Fellow, The Rockefeller University, New York, NY
- 1984-1986: Associate Physician, The Rockefeller University, New York, NY
- 1985-1986: Assistant Professor, The Rockefeller University, New York, NY
- 1986-1990: Assistant Professor, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX
- 1986-1991: Assistant Investigator, The Howard Hughes Medical Institute, Dallas, TX
- 1990-1996: Associate Professor, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX
- 1991-2000: Associate Investigator, The Howard Hughes Medical Institute, Dallas, TX
- 1996-2000: Professor, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX
- 2000-2011: Professor, Department of Immunology and Microbial Sciences, The Scripps Research Institute, La Jolla, CA
- 2007-2011: Chairman, Department of Genetics, The Scripps Research Institute, La Jolla, CA
- 2011-present: Raymond and Ellen Willie Distinguished Chair in Cancer Research, In honor of Laverne and Raymond Willie, Sr., UT Southwestern Medical Center, Dallas, TX

Solving New Phenotypes Induced by a Germline Mutagen in Real Time

Strange phenotypes have opened the way to discovery in almost every part of biomedicine. Many of these phenotypes were first observed in laboratory mice. Finding the mutation(s) responsible for phenotype was once an arduous task, requiring many years of work. Nonetheless, it was imperative to induce phenotype, screen for it, and ultimately solve it. During the past few years, the process has become highly automated, and within our laboratory, more than 150,000 germline coding/splicing changes have been made in the mouse and screened in the homozygous state to detect phenotypes that interest us. We have also devised a means of immediately determining which mutations cause those phenotypes that are observed. In this way, more than 1,500 phenotypic mutations have been declared. These mutations fall into more than 1,000 genes, and affect immunity, metabolism, neurobehavioral function, and other biological processes. Some screens have been pursued to the point that more than 35% of the genome has been examined in detail. A number of examples of new phenotypes and their causes will be presented.

Dinshaw J. Patel, Ph.D.

Abby Rockefeller Mauzé Chair in Experimental Therapeutics
Structural Biology Program
Memorial Sloan-Kettering Cancer Center
1275 York Avenue
New York, NY, 10065, USA

Professor Dinshaw Patel received his bachelor's degree in chemistry from the University of Mumbai in India and then moved to the United States for graduate school, completing a master's degree at the California Institute of Technology. He later recalled this experience, working in the laboratory of John D. Roberts, as his first exposure to NMR spectroscopy, a technique that would become a key part of his research program. Dr. Patel then joined the laboratory of David Schuster at New York University (NYU), from which he received his Ph.D. in chemistry. After completing his Ph.D., Dr. Patel became interested in moving from chemistry to biology and worked as a postdoctoral fellow with Robert Chambers at NYU. He then moved to Bell Labs in New Jersey, first as a postdoctoral researcher and later in a permanent position in polymer chemistry. He remained at Bell Labs for almost 17 years, primarily using NMR to study biological polymers.

In 1984, Dr. Patel moved from Bell Labs back to academia and became a professor of biochemistry and molecular biophysics at Columbia University Medical Center, where his research group focused on using NMR to study double-stranded DNA structures. He was recruited by Paul Marks at Memorial Sloan Kettering Cancer Center to move his laboratory and work to develop the institution's new program in structural biology, alongside colleague James Rothman. Following the move in 1992, Patel expanded his research interests into X-ray crystallography and RNA structure, and more recently into cryo-electron microscopy. Patel was elected to the National Academy of Sciences in 2009 and to the American Academy of Arts and Sciences in 2014.

Professor Patel's research focuses on structural biology of nucleic acids and has been particularly impactful in the study of RNA structure and protein-RNA interaction mechanisms. Patel's research group has studied riboswitches and ribozymes, as well as nuclease proteins involved in RNA interference processes. More recently his group has focused on the structural biology of epigenetic regulation, examining the mechanisms through which chemical modifications of DNA and histone proteins exert regulatory effects. The group also uses structural techniques to study innate immunity and lipid binding proteins. Professor Patel is an avid collector of Asian art.

Structural Biology of CRISPR-Cas Surveillance Complexes

Hui Yang, Ning Jia and Dinshaw J. Patel

The talk will focus on x–ray and cryo-EM structural studies of single-subunit type V (Cas12a and Cas12b), and multi-subunit type I-F (Csy) and III-A (Csm) CRISPR-Cas surveillance complexes in the absence and presence of anti-CRISPR proteins to deduce mechanistic insights into the assembly, target recognition, cleavage, inhibition and autoimmunity suppression of the CRISPR-Cas surveillance pathway.

Lieping Chen, MD, PhD
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Lieping Chen studies cell membrane proteins which control lymphocyte functions and translates his laboratory findings for the treatment of human diseases including cancer. Dr. Chen did the first proof-of-concept study in 1992 showing that the B7-CD28 family molecules could be the targets for cancer immunotherapy by introducing B7-1 into tumor cells to enhance therapeutic immunity. This study inspires subsequent studies targeting the B7-CD28/CTLA-4 family molecules for the treatment of cancer. Dr. Chen discovered B7-H1 (also called PD-L1) molecule in 1999 and demonstrated the role of PD-L1 in the evasion of immunity in tumor microenvironment. He singularly established the PD-1/PD-L1 pathway as the target for cancer immunotherapy in 1999-2002. He also initiated and help organized the first-in-man clinical trial of anti-PD-1 monoclonal antibody for treating human cancer in 2006 and developed PD-L1 staining as a biomarker to predict treatment outcome. His discoveries directly led to the development of anti-PD-1/PD-L1 antibody therapy against broad spectrum of human cancers (first approved in 2014 and five anti-PD-1/PD-L1 antibodies approved by US FDA since then). Dr. Chen's discoveries have revolutionized current oncology practice and cancer treatment.

Dr. Chen's laboratory also discovered various molecular pathways with immune modulatory functions and their applications in human disease treatment. These pathways include 4-1BB (CD137), ICOS/B7-H2, B7-H3, B7-H4, B7-H5/CD28H, PD-1H (VISTA), LIGHT/HVEM, TROY, B7-H2/CD28/CTLA-4 (human), SALM5/HVEM. These discoveries led to the development of therapeutic agents in various stages of clinical trials for the treatment of human diseases including cancer and autoimmune diseases.

Dr. Chen has published more than 350 research articles, review, book chapters and edited two books. His work in discovery of the PD-1/PD-L1 pathway in cancer therapy was cited as the #1 breakthrough of the years by *Science* magazine in 2013. He has received several awards and professional recognitions including William B. Coley Award (2014), Warren Alpert Foundation Prize (2017) and Giants of Cancer Care (2018).

A PARADIGM SHIFT IN CANCER IMMUNOTHERAPY: FROM ENHANCEMENT TO NORMALIZATION

Harnessing an antitumor immune response has been a fundamental strategy in cancer immunotherapy. For over a century, efforts have primarily focused on amplifying immune activation mechanisms which are employed by humans to eliminate invaders such as viruses and bacteria. This "immune enhancement" strategy (including IL-2, cancer vaccine and anti-CTLA-4 antibody) often results in rare objective responses and frequent immune-related adverse events (irAEs). However, in the last decade, cancer immunotherapies targeting the B7-H1/PD-1 pathway (anti-PD therapy), have achieved higher objective responses in patients with much fewer irAEs. This more beneficial tumor response-to-toxicity profile stems from distinct mechanisms of action that restore tumor-induced immune deficiency selectively in the tumor microenvironment, here termed "immune normalization" which has led to its FDA approval in more than 10 cancer indications and facilitated its combination with different therapies. I will highlight the principles of "immune normalization" and summarize what we have learned from it, with the ultimate goal to guide better designs for future cancer immunotherapies.

References:
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Zou WP, Wolchok JD and Chen L. Sci Transl Med 8:328rv4, 2016
Chen L and Han X. J Clin Invest 125(9):3384-3391, 2015

Xuetao Cao, M.D., Ph.D.

President, Nankai University, Tianjin, China;

Professor and Director, Center for Immunotherapy, Chinese Academy of Medical Sciences, Beijing, China;

Professor and Director, National Key Laboratory of Medical Immunology, Second Military Medical University (SMMU), Shanghai, China

Xuetao Cao received his M.D. and Ph.D. from Second Military Medical University (SMMU) (1986 and 1990, Shanghai, China). He became a full Professor of Immunology at SMMU in 1992, and served Chinese Academy of Medical Sciences as President during 2011-2017. Now, Dr. Cao is the President of Nankai University (Tianjin, China).

Dr. Cao's research focuses on innate immunity and inflammation, tumor immunotherapy. His group has made contributions to our understanding of innate signaling in immunity and inflammation, the identification of regulatory immune cell subsets and new molecular regulators in dendritic cell (DC)-initiated immune response, translational and clinical research of cancer immunotherapy. His group used unbiased approaches to screen DC for novel regulators of innate immunity. The functional characterization of these molecules revealed that innate sensors are regulated by degradation and trafficking, as well as by involvement of intracellular regulators or amplifiers. His studies demonstrated a complex interplay between innate signaling and other pathways that finely tunes host immune defense responses, inflammation resolution, and tumor surveillance. His group set up integrative approaches to improve outcome of cancer immunotherapy, and verified several potential biomarkers for prognosis and immunotherapy of human cancer patients.

Dr. Cao is the President of China Union of Life Science Societies, President of Chinese Society for Biomedical Engineering, Secretary General of Chinese Society for Immunology, Secretary General of Federation of Immunological Society in Asia and Oceania. He was elected as member of American Academy of Arts and Sciences (2018), US National Academy of Medicine (2017), UK Academy of Medical Sciences (2016), EMBO (2015), German Academy of Sciences (2013), Chinese Academy of Engineering (2005). As corresponding author, he has published more than 250 original papers in peer-reviewed journals including Cell, Nature, Science, Nature Immunology, Immunity, etc. He is the Founder Editor of *Chinese Journal of Cancer Biotherapy*, Co-Editor-in-Chief of *Cellular and Molecular Immunology*, Senior Editor of *Cancer Immunology Research*, and serves on the editorial board of journals such as *Cell, eLife, Cell Res,* etc.

Crosstalk of epigenetic modifiers and innate molecules in immunity and inflammation

Epigenetic regulators play essential roles in biological and pathological processes including immunity and inflammation. Epigenetic modifying factors and enzymes not only exert their “classical” role in controlling gene transcription, but also have the “non-classical” functions to regulate cellular signaling and responses. So, we are interested in the epigenetic regulation of the innate response and inflammation, and try to understand how the epigenetic regulators determine the developmental programs in the innate immune cells and tightly regulate the production and function of cytokines and inflammatory mediators in the inflammation and immunity. Furthermore, what’s the role of the epigenetic regulators in the host-pathogens interaction needs further investigation. The findings about the epigenetic regulators in the innate response and inflammation will be reported.

Liqun Luo, PhD
Ann and Bill Swindell Professor of Humanities and Sciences
Professor of Biology
Professor of Neurobiology by Courtesy
Stanford University
Investigator, Howard Hughes Medical Institute

Liqun Luo received BS from University of Science & Technology of China in 1986, PhD from Brandeis University in 1992, and did postdoctoral work at the University of California, San Francisco. He started his lab in the Department of Biology, Stanford University in 1996, where he has been a full professor since 2005. He has also been an investigator of the Howard Hughes Medical Institute since 2005.

Together with his students and postdocs, Dr. Luo studies how the brains are precisely wired up during development, and how neural circuits are organized to process information in adults. They have developed widely used genetic tools in flies and mice to label and genetically manipulate individual neurons in mosaic animals, and to gain genetic access to neurons activated by specific experience or behavioral episodes.

Dr. Luo has taught neurobiology to undergraduate and graduate students for the past 20 years. In 2015, he published a single-authored textbook, *Principles of Neurobiology*, which has since been translated into multiple languages and used in many universities around the world.

Dr. Luo has served on the editorial boards of scientific journals including *Neuron*, *eLife*, and *Annual Review of Neuroscience*, and on the selection committees of Pew Scholars, Damon Runyon Postdoctoral Fellows, and Future Prize. His honors include: Guo Mo-Ruo Prize, Sloan Award, McKnight Technological Innovation in Neuroscience Award, the Society for Neuroscience Young Investigator Award, Jacob Javits Award from National Institute of Neurological Disorders and Stroke, HW Mossman Award from American Association of Anatomists, and Lawrence Katz Prize. Dr. Luo is a Member of the National Academy of Sciences and a Fellow of the American Academy of Arts and Sciences.

Connections and communications between distributed neural circuits

In this talk I will present new studies on the development of connection specificity and information propagation in neural circuits across distant brain regions. The developmental part will focus on the extended hippocampal network. The functional part will discuss how thirst regulates motivated behavior.

Weimin Zhong, Ph.D., is an Associate Professor in the Department of Molecular, Cellular and Developmental Biology at Yale University. He attended Peking University as an undergraduate (premed) from 1981-1984 and studied medicine at Peking Union Medical College from 1984-1988. He joined the graduate program at The Rockefeller University afterwards and obtained Ph.D. in 1993. After postdoctoral training at University of California, San Francisco, he joined the Yale faculty in 1999. He was a former president of the Chinese Biological Investigators Society (2014-2016).

"Psychic" Stem Cells and the Connection between Regeneration, Degeneration and Cancer

We study why stem cells in mammalian tissues cannot repair damages caused by disease and injury, even though many contain stem cells capable of producing differentiated cells to repair normal wears and tears to maintain tissue function throughout life. We use the mammalian Numb proteins, Numb and Numblike (Numbl), as entry point, and neurogenesis in the developing neocortex and mammary gland growth during pregnancy as model systems, to probe the contribution of two modes of cell division – symmetric vs. asymmetric – in regulating stem cell behavior. Our findings reveal novel molecular pathways that specify the fates, count the number and regulate the temporal competence of neural stem cells. These pathways place fundamental constrains on the ability of stem cells to repair tissue damages and further reveal a connection between tissue regeneration, degeneration and cancer.

Xi He, PhD, is an Endowed Research Chair at the F. M. Kirby Center at Boston Children's Hospital (BCH) and Harvard Medical School (HMS).

Dr. He received his bachelor's degree in Mechanical Engineering and a Master degree in Bioengineering at Huazhong University of Science and Technology (HUST). Wuhan, China, and his PhD in biology in 1992 at University of California, San Diego, where in Dr. Michael G. Rosenfeld's lab he identified and studied a family of POU domain transcription factors in brain development. Dr. He did his postdoctoral training at National Institutes of Health (NIH) with Dr. Harold Varmus, and began his career on the study of Wnt signaling. At NIH he was trained and collaborated with Dr. Igor Dawid on vertebrate developmental biology.

Dr. He became an assistant professor in 1997 at BCH and HMS, and professor with tenure in 2007. Dr. He has pursued in understanding Wnt signaling in vertebrate development and human cancer/disease, and has identified many key components of and defined critical steps in this pivotal pathway. Dr. He was a Pew Scholar, Klingenstein Fellow, W.M. Keck Distinguished Young Scholar, and Scholar of the Leukemia and Lymphoma Society. Dr. He received the Young Investigator Award from the Society of Chinese Bioscientists in America (SCBA) in 2004, and was named an American Cancer Society Research Professor in 2015. Dr. He was a Board member of CBIS and serves currently as the Executive Co-Director of SCBA. Dr. He has been on numerous review and advisory panels in academia and the biopharmaceutical industry in the US, China, EU, and UK. His research continues to focus on Wnt signaling in development, stem cell, and cancer/disease using models ranging from Xenopus, mice, to human (normal and cancer) organoids.

Wnt signaling in vertebrate development and stem cell biology

Signal transduction by the Wnt family of secreted lipoproteins is essential for animal development and tissue homeostasis, and abnormal Wnt signaling is associated with and causes many human diseases including cancer. Our research focuses on understanding the mechanism of Wnt signal transduction in vertebrate development and human diseases. We are particularly interested in the molecular logic of Wnt signaling pathways, in regulation of embryonic pluripotency and patterning in Xenopus and mouse embryos, and in modeling human cancer and diseases using mouse genetics and human organoids.

At the meeting I will present our effort to identify new components of Wnt signaling using CRISPR/Cas9-based genome-wide screening, and new insights into human diseases/cancer.

- **王晓东**

北京生命科学研究所所长，百济神州创始人，美国科学院院士，未来论坛科学家委员会委员

Xiaodong WANG

Director & Investigator, National Institute of Biological Sciences, Beijing, Academician, American National Academy of Sciences; Member, the Scientist Committee of Future Forum

Xiaodong Wang is currently the Director and Investigator of National Institute of Biological Sciences, Beijing. He received his B.S. degree from Beijing Normal University and his Ph.D. degree of Biochemistry from University of Texas Southwestern Medical Center at Dallas. After his postdoctoral training at the Department of Molecular Genetics at the same school, he started his independent research career at Emory University in Atlanta. He returned to UT-Southwestern in 1996 as a faculty member at the Department of Biochemistry and held the position of George MacGregor Distinguished Professor until he returned to Beijing to take his current position in 2010. He was also an Investigator of Howard Hughes Medical Institute from 1997 to 2010. Xiaodong Wang's research centers on the biochemical understanding of programmed cell death in mammalian cells. Their laboratory is responsible for the discovery of the role of cytochrome c in apoptosis that established the signaling function of mitochondria. Their more recent work identified RIP3 kinase and its substrate MLKL as the core components of a pathway controlling and executing programmed necrosis. For his research achievements, Xiaodong Wang was elected to be a member of National Academy of Sciences, USA; Foreign-associate member of Chinese Academy of Sciences and European Molecular Biology Organization.

王晓东博士1963年出生于中国武汉，1984年毕业于北京师范大学，1991年获美国得克萨斯州西南医学中心生物化学博士。现为北京生命科学研究所资深研究员，所长。自1995年以来，王晓东博士主要致力于人体细胞凋亡的研究，凋亡是细胞的一种特殊生理功能，对人体正常发育和清除损伤细胞起着至关重要的作用。凋亡的缺陷是肿瘤发生的关键步骤。在过去的十几年中，王晓东博士领导的实验室发现了细胞凋亡的生化通路与其作用机理。根据这些研究成果，王晓东博士还研发出针对肿瘤细胞凋亡的新型实验性肿瘤治疗药物。王晓东博士2004年被评为美国科学院院士，2013年入选中国科学院外籍院士，并获得多项国际生物研究奖，其中包括2006年的"邵逸夫生命科学与医学奖"。

Charlene Liao, PhD 廖晓伶博士

Charlene Liao, Ph.D., co-founded Immune-Onc Therapeutics and has served as its President and Chief Executive Officer and as a member of its board of directors since May 2016. Charlene has 22 years of industry experience in drug development and business leadership. From 2002-2016, Charlene held global drug development roles at Genentech where she was instrumental in leading development efforts across the product lifecycle for ten new molecular entities (NMEs) in a variety of therapeutic areas including immunology, infectious diseases, metabolic disorders, neuroscience and oncology. Prior to joining Genentech, Charlene was a Director of Business Development at Rigel. She began her career in biotech as a scientist at Tularik, before its acquisition by Amgen.

Charlene holds a B.S. in Biochemistry from Peking University in China and received her Ph.D. from Brandeis University in the laboratory of famed biologist Dr. Michael Rosbash, who was awarded the 2017 Nobel Prize in Physiology or Medicine. Charlene completed her postdoctoral research in immunology at UCSF where she was a Fellow of the Damon Runyon Cancer Research Fund in the laboratory of Dr. Dan Littman and a Special Fellow of the Leukemia and Lymphoma Society (LLS) in the laboratory of Dr. Art Weiss.

廖晓伶博士毕业于北京大学生物系本科；保送北大研究生院；通过CUSBEA（中美分子生物学生物化学联合招生）选拔赴美到布兰迪斯大学获哲学博士学位，师从2017年诺贝尔奖得主 Michael Rosbash；后进入加州大学旧金山分校进行博士后研究。2013 年5月获美国斯坦福商学院高管培训。

廖晓伶博士2002年起任美国基因泰克Genentech Inc. 药物开发高级项目领导，成功领导多种创新药物的临床研发，包括小分子和 大分子药品，也包括癌症，免疫，代谢，神经，病毒及其他多种疾病的药物开发。基因泰克自2009年为瑞士跨国公司罗氏并购。廖晓伶在2011和2012分别代表罗氏和基因泰克接待中国驻旧金山总领事馆，中国国家科技部，卫生部和药监部的访问并介绍创新经验。

廖晓伶于2016年5月离开基因泰克，在硅谷组建创新生物医药公司 Immune-Onc Therapeutics, Inc. 并担任总裁兼首席执行官。她目前是北京大学生命科学院尊师基金理事会成员，以及华人生物学家协会 (CBIS) 理事会成员。

Steve Q. Yang, Ph.D. 杨青博士

Dr. Steve Yang is Executive Vice President and Chief Business Officer of WuXi AppTec. His responsibilities include management of multiple business units and commercial operation. WuXi AppTec is a leading global pharmaceutical, biopharmaceutical, and medical device R&D capability and technology open access platform company with operations in China, US, and Europe.

Dr. Yang is a pharmaceutical industry leader recognized for building R&D and service capabilities, delivering research and early development portfolios of drug candidates, and establishing R&D partnerships in US, Europe, China and other Asian and emerging markets. Before joining WuXi, Dr. Yang was Vice President and Head of Asia and Emerging Markets iMed at AstraZeneca, based in Shanghai. Previously, Dr. Yang served as Vice President and Head of Asia R&D at Pfizer based in Shanghai, and as Executive Director and head of Pfizer's global R&D strategic management group based in the United States.

Dr. Yang received his PhD in Pharmaceutical Chemistry from the University of California, San Francisco. He started his undergraduate study in Fudan University, China and completed his BS Summa Cum Laude from Michigan Technological University. He co-founded the BayHelix Group, a non-profit global professional organization of Chinese life science business leaders, and served as the chairman of the board for two terms.

杨青博士现任药明康德新药开发有限公司执行副总裁及首席商务官，负责公司多个业务部门及商业运营的工作。药明康德是全球领先的制药、生物技术以及医疗器械开放式研发服务平台公司，在中美两国及欧洲均有运营实体。

杨青博士在建立医药研发及服务能力，开发候选药物的研究和早期临床，以及在欧美，中国，亚洲以及其他新兴市场建立研发合作等方面，被誉为医药行业的领军人物。在加入药明康德之前，杨博士曾担任阿斯利康制药公司亚洲及新兴市场创新医药研发副总裁。在加入阿斯利康之前，杨博士曾担任辉瑞制药公司的亚洲研发副总裁和辉瑞全球研发战略管理部负责人和部门执行总监。

杨博士本科曾就读于复旦大学，以最优等生从美国密西根理工大学获得生物学学士学位，并于美国加州大学旧金山分校获得药物化学博士学位。杨博士是百华协会的共同创始人之一，并曾担任两届董事会主席。百华协会是由全球生命科学和医药领域的杰出华人商业领袖所组成的非盈利性组织。

Zhizhong Li, Ph.D. 李治中博士

Dr. Zhizhong Li is currently the co-founder of Shiyu Children Foundation, a NGO focusing on promoting awareness, patient education and drug discovery for pediatric cancers. He is also a best-selling author and has written three books on the topic of cancer biology and oncology drug discovery. His books have won over 10 prestigious awards in China, including "Best 30 Books in China 2015" and "Best Pop Science Book in China 2017". His WeChat blog has over 500,000 followers.

Dr. Zhizhong Li graduated from Duke University with PhD in Molecular Cancer Biology, before joining Novartis (NIBR) as a presidential postdoc fellow. In 2013, He joined Novartis Institutes for BioMedical Research as a research investigator in the department of Oncology Drug Discovery, focusing on new target identification and validation. He published over 20 peer-reviewed research articles including a cover story on Cancer Cell. His work has been cited for over 6000 times.

中文简介：

李治中，清华大学生物系本科，美国杜克大学癌症生物学和药理学博士。现任美国诺华制药实验室负责人，负责新型癌症靶向和免疫新药研发。发表研究论文20余篇，包括顶尖杂志Cancer Cell 封面文章，Dev Cell等，引用超过6000次。

笔名"菠萝"，著有科普畅销书《癌症.真相：医生也在读》，销量超20万册，被誉为"近年中国最好的原创科普书之一"。荣获2015年中国图书评论协会/央视"中国好书奖"，国家图书馆第十一届"文津图书奖"，第八届吴大猷科普著作奖。

2017年新书《癌症·新知：科学终结恐慌》由吴一龙、冯唐、李一诺、姬十三、魏坤琳、张晓龙等联合推荐，荣获中国出版协会2017年度好书，中国科普作家协会优秀科普作品金奖，深圳市2017十大好书等多项大奖。

运营科普公众号"健康不是闹着玩儿"和"菠萝因子"，订阅人数近50万。联合发起深圳市拾玉儿童公益基金会并担任秘书长，发起儿童癌症专业公益项目："向日葵儿童"。

尚立斌博士

尚立斌，1980 年 2 月生，南京大学理学学士和硕士（生物化学专业），2011 年获得美国得克萨斯大学西南医学中心博士学位（生物化学专业），博士期间的学术研究领域主要在哺乳动物细胞自噬的启动机制。

尚立斌博士回国后主要从事商务发展及业务运营相关工作，2011 年加入中国五矿，先后任五矿发展股份有限公司投资管理部部门经理、五矿供应链（深圳）有限公司副总经理等职务，负责大宗商品投资项目的策划评审和现货贸易。2016 年，尚立斌博士加入百济神州（北京）生物科技有限公司任业务拓展总监，参与百济神州大分子生物药生产基地项目谈判。2017 年，尚立斌博士担任百济神州生物药业有限公司业务运营副总裁，牵头负责百济神州大分子生物药商业化生产平台项目的落地对接和业务运营。

曹德骏

Jacky Cao, Sr. business development manager of MS-Life Science & Tissue Diagnostics Of Roche Diagnostics China. Jacky Cao graduated from Peking Union Medical College in 2002 with a focus on stem cells and related applications. After graduation, he has joined Abbott, bioMérieux, BD, Bio-Rad and Thermo Scientific, and is responsible for molecular biology, cell biology, immunology, microbiology, etc. with rich experiences of research, sales and marketing and management in R&D and IVD industries. In 2018, he joined the department of MS-Life Science & Tissue Diagnostics of Roche Diagnostics China and is responsible for the business development of new molecular technologies and products in the market of research, industrial and diagnostic.

曹德骏，现任罗氏诊断中国公司分子解决方案-生命科学和组织诊断部资深商务发展经理。曹德骏于2002年毕业于北京协和医科大学，研究课题聚焦干细胞及相关应用。毕业后陆续加入了美国雅培公司、法国生物梅里埃公司、美国碧迪公司、美国伯乐公司以及美国赛默飞公司，负责的业务领域涵盖了分子生物学、细胞生物学、免疫学、微生物学等多个领域，具备丰富的科研及IVD行业的销售、市场及管理经验。2018年加入了罗氏诊断公司中国区分子解决方案-生命科学和组织诊断部，负责开拓罗氏诊断公司最新分子生物学技术和产品在科研、工业及诊断领域的应用

Jiahuai Han, PhD
Professor, School of Life Sciences and School of Medicine
Director, State Key Laboratory of Cellular Stress Biology
Xiamen University, China

Education:

- BS (1982), Peking University, China, Specialty in Biochemistry
- MS (1985), Peking University, China, Specialty in Protein Chemistry
- PhD (1990), University of Brussels (Université Libre de Bruxelles), Belgium, Specialty in Molecular Biology

Research and Professional Experience:

1987 – 1992 Research Fellow, Department of Internal Medicine and Howard Hughes Medical Institute, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA
1992 – 1993 Research Associate, Department of Immunology, The Scripps Research Institute, La Jolla, California, USA
1993 – 1996 Assistant Member, Department of Immunology, The Scripps Research Institute, La Jolla, California, USA
1996 – 2004 Associate Professor, Department of Immunology, The Scripps Research Institute, La Jolla, California, USA
2004 – 2007 Professor, Department of Immunology, The Scripps Research Institute, La Jolla, California, USA
2002 – 2007 Adj. Professor, School of Life Sciences, Xiamen University, Xiamen, China
2007- Professor, School of Life Sciences
2007- Adj. Professor, Department of Immunology, The Scripps Research Institute, La Jolla, California, USA

Research Interests:

Dr. Jiahuai Han is known for the discovery of the p38 signaling pathway, one of the most important pathways in intracellular signaling transduction. This pathway plays important roles in many biological processes including immunity, development and tumorigenesis. Another current focus of Han lab is molecular mechanisms of programmed necrosis and the immune responses elicited by necrotic cell death. Han Lab is one of the laboratories that discovered the role of RIP3 and GSDMD in necroptosis and pyroptosis, respectively. Han Lab is also interested in recognition and tolerance of invasive viruses and tumor cells.

Representative Publications (not more than 5):

1. He WT, et al. Gasdermin D is an executor of pyroptosis and required for interleukin-1β secretion. Cell Res. 2015 Dec; 25(12): 1285-98.
2. Zhang DW, et al. RIP3, an energy metabolism regulator that switches TNF-induced cell death from apoptosis to necrosis. Science. 2009. 325: 332-6
3. Sun P, et al. PRAK is essential for ras-induced senescence and tumor suppression. Cell. 2007 128: 295-308
4. Han J, et al. Activation of the transcription factor MEF2C by the MAP kinase p38 in inflammation. Nature. 1997 386: 296-9
5. Han J, et al. A MAP kinase targeted by endotoxin and hyperosmolarity in mammalian cells. Science. 1994 265: 808-11

Quantitative analysis of signaling pathways in inflammatory cell activation

Dynamical formation of signaling complexes is the most important regulatory mechanism in control of diverse cellular processes including cellular activation in inflammation. Although the levels of the activation of signaling pathways play a key role in regulating cell functions, the related study is very limited due to difficulties in quantitative analysis of signaling pathways. Tagging signaling protein with common used epitope such as Flag in culture cells has made immune-purification of a variety of signaling complexes feasible and reproducible. The high sensitive quantitative MS technique made it possible to collect quantitative data of proteins in the signaling complexes. We analyzed the assembling of different signaling complexes in cells treated with LPS or TNF. Extraction of quantitative information from the MS data of multiple time course samples was performed by our software named Group-DIA. The software utilizes information of elution profiles to generate pseudo-spectra, thereby greatly improving the accuracy of match between the precursor ions and product ions. Through these analyses, we were able to show the dynamic assembling of signaling complexes and obtained some previously unknown information of these signaling pathways.

Guoliang Xu, PhD

Principal Investigator, Institute of Biochemistry and Cell Biology, CAS & Fudan University Medical School. Shanghai. China

Education:

- BS (1985) Dept Biology, Zhejiang University, China
- MS (1988) Institute of Genetics, Chinese Academy of Sciences, China
- PhD (1993) Max Planck Institute (MPI) for Molecular Genetics & Technical University Berlin, Germany
- Postdoc (1995-2001) Dept of Genetics & Development, Columbia University, US

Other Positions:

- Editorial Board: *J Biol Chem*, *Development*

Research Interests:

- DNA modifications, DNA methylation, nucleotide metabolism, epigenetics, leukemia, meiosis, CRISPR

Representative Publications (not more than 5):

Hai-Qiang Dai, Bang-An Wang, Lu Yang, Jia-Jia Chen et al., Xin Sun & **Guo-Liang Xu** (2016) DNA demethylation by TET dioxygenases controls gastrula patterning by regulating Lefty-Nodal signaling. ***Nature*** 538, 528–532.

Fan Guo et al., Jin-Song Li, Fuchou Tang et al. & **Guo-Liang Xu** (2014) Active and passive demethylation of male and female pronuclear DNA in the mammalian zygote. ***Cell Stem Cell*** 15, 447–458.

Hu X, et al., **Xu GL**. (2014) Tet and TDG Mediate DNA Demethylation Essential for Mesenchymal-to-Epithelial Transition in Somatic Cell Reprogramming. ***Cell Stem Cell*** 14, 512–522.

Tian-Peng Gu, Fan Guo, Hui Yang, et al., Jinsong Li and **Guo-Liang Xu** (2011) The role of Tet3 DNA dioxygenase in epigenetic reprogramming by oocytes. ***Nature***, 477, 606–610.

Yu-Fei He, Bin-Zhong Li, et al., **Guo-Liang Xu** (2011) Tet-mediated formation of 5-carboxylcytosine and its excision by TDG in mammalian DNA. ***Science*** 333, 1303–1307.

A vitamin C-derived DNA modification catalyzed by a TET-related oxidase mediates epigenetic regulation of photosynthesis

Methylation of cytosine to 5-methylcytosine (5mC) is a prevalent DNA modification found in many organisms. Sequential oxidation of 5mC by TET dioxygenases results in a cascade of additional epigenetic marks and promotes DNA demethylation in mammals. However, the enzymatic activity and the function of TET homologs present in lower eukaryotes remains largely unexplored. In our study of TET homologs in the green alga *Chlamydomonas reinhardtii* (*C. reinhardtii*), we have found a 5mC-modifying enzyme (CMD1) that catalyzes conjugation of a glyceryl moiety onto the methyl group of 5mC through a carbon-carbon bond, resulting in two novel stereoisomeric nucleotide products. The catalytic activity of CMD1 requires Fe(II) and the integrity of its His-x-Asp (HxD) binding motif, which is conserved in Fe-dependent oxygenases. However, unlike all previous described TET enzymes which utilize 2-oxoglutarate (2-OG) as a co-substrate, CMD1 utilizes L-ascorbic acid (vitamin C, VC) as an essential co-substrate. VC itself is the source of the glyceryl moiety that modifies 5mC, with concurrent formation of glyoxylic acid and CO_2. The VC-derived DNA modification is present in the genome of *C. reinhardtii* and its level decreases significantly in a *CMD1* mutant strain. The fitness of *CMD1* mutant cells to high light exposure is reduced, mainly due to deficient expression of the critical non-photochemical quenching (NPQ) effector gene *LHCSR3*, which is hypermethylated in the mutant cells. Our study thus reveals a new eukaryotic DNA base modification, and its involvement in a functionally conserved but mechanistically divergent DNA demethylation pathway for the epigenetic regulation of photosynthesis. The potential response of DNA repair machinery to the bulky cytosine base modification will also be discussed.

Ye-Guang Chen, Ph.D.

Dr. Ye-Guang Chen, a professor at Tsinghua University, received his PhD degree from Albert Einstein College of Medicine in 1996. After trained in Memorial Sloan-Kettering Cancer Center as a Howard Hughes Medical Institute postdoctoral research associate from 1996 to 2000, he was recruited to the University of California, Riverside as a tenure-track assistant professor, and then joined Tsinghua University as a Chung Kong Scholar in 2002. He received the National Science Foundation for Outstanding Young Scientist of China. He was honored with the Li Foundation Heritage Prize for "Excellence in Creativity" (New York) and Ho Leung Ho Lee Foundation Prize for Scientific and Technological Progress, and elected to the Chinese Academy of Sciences in 2017. He is currently serving as the president of the Chinese Society of Cell Biology and has been on the Editorial Board of *Journal of Biological Chemistry, Cell Research, Biochemical Journal* and other journals. His research interests concern on how TGF-beta signaling is regulated, aiming to understand the role of TGF-beta in stem cell biology, tissue homeostasis and related diseases. He is also interested in how Wnt signaling is modulated.

Modulation of TGF-β signaling

Transforming growth factor-β (TGF-β) is a multi-functional cytokine and controls cell proliferation, differentiation, migration and death. Deregulation of its signaling has been associated with different types of diseases, including cancer. Its signaling activity is modulated by many factors and at different levels. We have been focusing on how TGF-β receptor stability and Smad activity are regulated by endocytosis and by other signal pathways. In this talk, I will show how TGF-β receptor stability is modulated by its subcellular localization and DNA damage. I will also discuss how HER2/EGFR signaling can switch TGF-β function in breast cancer cells from anti-proliferation to cancer promotion.

Haifan Lin, Ph.D.

Eugene Higgins Professor of Cell Biology, Professor of Genetics, of Obstetrics, Gynecology, and Reproductive Sciences, and of Dermatology;
Founding Director, Yale Stem Cell Center;
Founding Dean (adjunct), School of Life Science and Technology, ShanghaiTech University.

Dr. Lin received his BS degree from Fudan University, PhD degree from Cornell University, and postdoctoral training at the Carnegie Institution for Science. He joined the faculty of Duke University Medical School in 1994, where he rose to Full Professor. He founded and directed the Duke Stem Cell Research Program (2005-2006), the Yale Stem Cell Center (2006-present), and School of Life Science and Technology at ShanghaiTech University (2014-present).

Dr. Lin studies the self-renewing mechanism of stem cells, stem cell-related cancers, and reproductive biology. He made key contributions to the demonstration of stem cell self-renewing division and the proof of the stem cell niche theory. He discovered the Argonuate/Piwi gene family and their essential function in stem cell self-renewal and germline development. He is also a discoverer of PIWI-interacting RNA (piRNA), a discovery hailed by Science as one of the 10 Breakthroughs in 2006. Recently, he demonstrated the crucial roles of the Piwi-piRNA pathway in epigenetic programming and post-transcriptional regulation of mRNA and lncRNA.

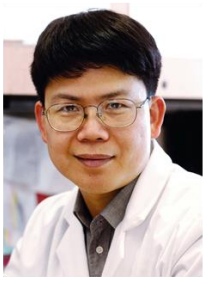
Dr. Lin has served in numerous leadership roles in the scientific community and beyond, including the Board of Director (2009-present), Treasurer (2013-2016), and Executive Committee (2013-2016) of the International Society for Stem Cell Research (ISSCR), Chairman of ISSCR Finance (2013-2016), Publication (2009-2012), and Annual Meeting Program Committees (2010-2011). He also served on the NIH Director's Pioneer Award Committee (2009), the Medical Advisory Board of New York Stem Cell Foundation (2009-present), RIKEN CDB Advisory Council (2007-2016), Visiting Chair Professorship at Tsinghua University (2002-present), Advisory Board of Connecticut Innovation (2017-present), Advisor of World Wenzhou People Association (2007-present), and other responsibilities.

Dr. Lin received more than 30 awards in his career, including the NIH Director's Pioneer Award (2010), the NIH MERIT Award (2012), the Ray Wu Award from the Chinese Biological Investigators Society (2013), and the Society for the Study of Reproduction Research Award (2015). He is a Member of US National Academy of Sciences, a Member of American Academy of Arts and Sciences, and a Fellow of the American Association for Advancement of Science.

Piwi Proteins and piRNAs: A new paradigm in Gene Regulation

Small non-coding RNAs have been recognized as key players in gene regulation. In 2006, we and others independently discovered a novel class of small RNAs that interact with Piwi proteins in the germline of diverse organisms. These Piwi-interacting RNAs (piRNAs), mostly 26-32 nucleotide in length and correspond to all types of genomic sequences, represent a distinct small-RNA pathway. In my talk, I will report our recent progress that reveal the crucial roles of the Piwi-piRNA pathway in guiding targeted epigenetic modification of the genome and in mediating the regulation of mRNA and lncRNA stability by transposons and pseudogenes.

Key words: Piwi; Argonaute; piRNA; germline; epigenetics; posttranscriptional regulation.



Zhijian 'James' Chen, Ph.D.
Investigator, Howard Hughes Medical Institute
George MacGregor Distinguished Chair in Biomedical Sciences
Director, Center for Inflammation Research
Professor, Department of Molecular Biology
University of Texas Southwestern Medical Center

E-mail: zhijian.chen@utsouthwestern.edu

Zhijian 'James' Chen received his B.S. degree in Biology in 1985 from Fujian Normal University and his Ph.D. degree in Biochemistry in 1991 from the State University of New York at Buffalo. After his postdoctoral training at the Salk Institute, Chen joined Baxter Healthcare in 1992 as a Research Scientist to work on Cancer Immunotherapy. In 1994, Chen became a Senior Scientist at ProScript Inc, a start-up biotechnology company where he helped discover the proteasome inhibitor VELCADE, a medicine used for the treatment of multiple myeloma and mantle cell lymphoma. In 1997, Chen joined UT Southwestern as an Assistant Professor and became a Professor in 2015. Since 2015, Chen has been an Investigator of Howard Hughes Medical Institute. He is also George L. MacGregor Distinguished Chair in Biomedical Science and Director of Inflammation Research Center at UT Southwestern.

Chen has made a series of discoveries that transformed our understanding of cell signaling and innate immunity. These discoveries include the regulatory role of ubiquitination in protein kinase activation in the NF-kB and MAP kinase pathways, the Mitochondrial Antiviral Signaling (MAVS) protein that reveals a new role of mitochondria in immunity, and more recently, cyclic GMP-AMP synthase (cGAS) as the long-sought cytosolic DNA sensor and a new cyclic di-nucleotide signaling pathway that mediate innate immune responses in animal cells.

For his work, Chen has received numerous honors, including the National Academy of Science Award in Molecular Biology (2012), the American Society of Biochemistry and Molecular Biology (ASBMB) Merck Award (2015), and the Lurie Prize in Biomedical Sciences (2018). Chen is a member of the National Academy of Sciences.

The cGAS-STING pathway of Innate Immunity

The presence of DNA in the cytoplasm is a danger signal that alerts the host immune system to eliminate microbial infections, but inappropriate activation of this pathway by self DNA can also lead to autoimmune and autoinflammatory diseases. My talk will focus on our discoveries of cyclic GMP-AMP synthase (cGAS) as an innate immune sensor for cytosolic DNA, and of cyclic GMP-AMP (cGAMP) as a second messenger that triggers the production of type-I interferons and other inflammatory cytokines. I will also discuss our recent work on the regulation of cGAS and its role in cellular senescence and cancer immunotherapy.

Xinnian Dong, Ph.D.
HHMI Investigator
Arts & Sciences Professor of Biology
Duke University, NC, USA
E-mail: xdong@duke.edu

Xinnian Dong received her B.S. degree in microbiology from Wuhan University in China in 1982 and came to the US to pursue her graduate degree in the same year. Xinnian Dong was awarded Ph.D. degree in molecular biology by Northwestern University in Chicago in 1988. She became interested in using *Arabidopsis thaliana* as model organism to study plant immune mechanisms when she was a postdoctoral fellow with Dr. Fred Ausubel at Massachusetts General Hospital in Harvard Medical School. Xinnian Dong became an Assistant Professor at Duke University in 1992 and was promoted to Associate Professor in 1999 and Full Professor in 2004. She is currently an Arts & Sciences Distinguished Professor of Biology (since 2007).

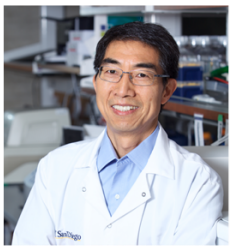
The Dong laboratory identified NPR1, a master regulator of immune regulator in plants, and made several important discoveries on how NPR1 transduces the immune signal salicylic acid in conferring broad-spectrum disease resistance. In recent years, the Dong lab discovered surprising connections between plant defense with the circadian clock and with the DNA damage repair machinery. Moreover, they found that translational regulation is a critical step of immune induction and controlling translation of master immune regulators, such as NPR1, in a pathogen inducible manner can render broad-spectrum disease resistance to rice without any significant yield penalty normally associated with enhanced immunity.

Xinnian Dong became a HHMI investigator in 2011, elected as an AAAS fellow in 2011, a member of the National Academy of Sciences in 2012 and an American Academy of Microbiology Fellow in 2013. She was also named as an outstanding alumna of Wuhan University in the same year.

Breaking the Disease Triangle by the Circadian Clock

Musoki Mwimba[1], Wei Wang[1], Mian Zhou[1], Sargis Karapetyan[1,3], Nick Buchler[2,3], Xinnian Dong[1]

The outbreak of a disease is determined by interactions between the host, its environment and the pathogen. This “disease triangle” model has been used to predict epidemics in humans as well as in agricultural plants. Because plants are sessile organisms, every aspect of the plant physiology, including immunity against pathogens, is influenced by the environmental conditions, such as light, temperature, and humidity. Moreover, in the absence specialized immune cells, plant defense occurs in coordination with plant growth. In my talk, I will discuss the intricate interconnections between the circadian clock and plant immune mechanisms. I will then show how circadian clock integrates environmental signals in timing as well as gating immune responses to protect against infection while avoiding conflicts with growth-related activities.



Kun-Liang Guan, Ph.D.
Distinguished Professor of Pharmacology
University of California, San Diego (UCSD).

Kun-Liang Guan received his B.S. (1982) from Hangzhou University, China and his Ph.D. (1989) from Purdue University, USA. He did his postdoctoral training also at Purdue University, where he discovered the dual specific phosphatase family and a novel biochemical catalysis via thio-phosphate intermediate. From 1992-2007, Dr. Guan was a faculty in the Department of Biological Chemistry and Life Sciences Institute at the University of Michigan (from assistant professor to the Halvor Christensen Professor). In 2007, Dr. Guan moved to the Department of Pharmacology, University of California, San Diego (UCSD).

Dr. Guan's research focuses on signal transduction in cell growth regulation and tumorigenesis. Works from his laboratory have made major contributions to the establishment of the mTOR signaling network, including the demonstration of the TSC1 and TSC2 tumor suppressors as essential regulators of the mTOR kinase, and linking growth factor, energy and nutrient signals to mTOR regulation and cell growth. Recent works from the Guan group have defined the molecular/biochemical regulation and upstream signals of the emerging Hippo pathway that controls tissue homeostasis and organ size.

Guan received the John D. & Catherine T. MacArthur Foundation MacArthur Fellowship (1998), the American Society of Biochemistry and Molecular Biology Young Investigator Award (1999), Distinguished Alumni Award (2006) from Purdue University, Ray Wu Award from CBI Society (2011), and Fellow of AAAS (2011). He is one of the most highly cited researchers in molecular biology and genetics (H-index 117, Thomson Reuters) and has co-authored over 300 peer-reviewed scientific papers.

Xiang-Dong Fu, PhD
Professor of Cellular and Molecular Medicine, University of California, San Diego, USA

Xiang-Dong Fu received his B.S. degree of Virology from Wuhan University in 1982. He was the first class of the CUSBEA (China-United States Biochemistry Examination and Application) program to enter the US for graduate training. He did his graduate work with Jonathan Lis on retroviral replication and received his Ph.D. degree in Biochemistry from Case Western Reserve University in 1988. He subsequently joined Tom Maniatis lab for postdoctoral training on pre-mRNA splicing at Harvard in 1988. In 1992, he joined the faculty at U niversity of California, San Diego and rose through the rank (Assistant Professor, 1992-1998; Associate Professor with tenure, 1998 to 2002; and Full Professor, 2002-present). He became a Distinguished Professor of Cellular and Molecular Medicine in 2018 at UC, San Diego.

Throughout his academic career, Dr. Fu made fours sets of key discoveries: (1) He used partially purified spliceosome to raise a large panel of monoclonal antibodies, which led to the discovery of the first non-snRNP splicing factor SC35, a founding of the SR family of splicing regulators. He conducted a large body of functional and mechanistic studies on SR proteins, revealing their central roles in key developm ental and disease processes by committing pre-mRNA to the splicing pathway and regulating alternative splicing in dosage-dependent and position-sensitive manner. (2) His group was also responsible for the discovery of the SRPK family of splicing kinases highly specific for SR proteins and elucidates a dedicated signaling pathway via these kinases to transduce growth factor signaling to the nucleus to regulate alternative splicing. (3) He pioneered studies on cell fate switches mediated by regulatory RNAs and RNA binding proteins and elucidated an RNA program necessary and sufficient to trans-differentiate fibroblasts into functional neurons. (4) Using the newly developed neuronal conversion strategy, he directly converted astrocyte into functional neurons in the brain and demonstrated that those newly converted neurons are functionally integrated into the exis ting neuronal circuitry. On a chemical-induced Parkinson's disease mouse model, he demonstrated that such trans-differentiated neurons are able to reconstitute the nigrostriatal dopamine pathway, thereby completely eradicating the Parkinson's Disease phenotype. These findings suggest a new and general strategy to combat various forms of neurodegenerative diseases.

Dr. Fu's contributions to biomedical research have been honored by selectionas Searle Scholar (1994), Leukemia and Lymphoma Society Scholar (1997), Distinguished Alumnus of Wuhan University (2003), Prostate Cancer Foundation Challenge Award (2008), election to AAAS Fellow (2010). and the Ray Wu Society Award (2016).

Junjie Chen, PhD
Professor and Chair
Department of Experimental Radiation Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Education:

- BS (1988), Genetics and Genetic Engineering, Fudan University
- PhD (1994), Cell and Molecular Biology, University of Vermont
- Postdoctoral training (1994-1996), Dept. of Pathology, Harvard Medical School, Brigham & Women's Hospital
- Postdoctoral training (1996-1999), Dept. of Cancer Biology, Harvard Medical School, Dana-Farber Cancer Institute

Other Positions:

- Senior Editor, Cancer Research.

Research Interests:

DNA repair, DNA damage checkpoints, tumor suppressors, oncogenes, proteomics

Representative Publications (not more than 5):

•Chen Z, Tran M, Tang M, Wang W, Gong Z, **Chen J.** Proteomic Analysis Reveals a Novel Mutator S (MutS) Partner Involved in Mismatch Repair Pathway. Mol Cell Proteomics 15(4):1299-308, 4/2016.

•Li X, Tran KM, Aziz KE, Sorokin AV, **Chen J***, Wang W* (*Corresponding authors). Defining the protein-protein interaction network of the human protein tyrosine phosphatase family. Mol Cell Proteomics 15(9):3030-44, 9/2016.

•Lee YC, Zhou Q, **Chen J***, Yuan J* (*Corresponding authors). RPA-Binding Protein ETAA1 Is an ATR Activator Involved in DNA Replication Stress Response. Curr Biol 26(24):3257-3268, 12/2016.

•Li X, Gao M, Choi JM, Kim BJ, Zhou MT, Chen Z, Jain AN, Jung SY, Yuan J, Wang W, Wang Y, **Chen J**. CRISPR/Cas9-Coupled Affinity Purification/Mass Spectrometry Analysis Revealed a Novel Role of Neurofibromin in mTOR Signaling. Mol Cell Proteomics. e-Pub 2/2017.

•Zhang A, Peng B, Huang P, **Chen J***, Gong Z* (*Corresponding authors). The p53-binding Protein 1-Tudor Interacting Repair Regulator Complex Participates in the DNA Damage Response. J Biol Chem. e-Pub 2/2017.

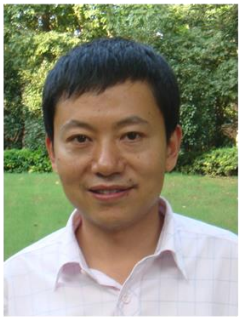
Targeting DNA damage repair in cancer therapy

DNA double strand breaks (DSBs) are repaired by nonhomologous end joining (NHEJ) and homologous recombination (HR) pathways in mammalian cells. It is speculated that which pathway to use for DSB repair is mainly controlled by end resection process. This repair pathway choice is important for tumor response to PARP inhibition, which is now accepted therapeutic strategy for cancer patients carrying BRCA mutations. While BRCA1 promotes end resection and therefore favors HR repair, 53BP1 inhibits end resection and engages NHEJ pathway for DSB repair. We and others showed previously that RIF1 is a major downstream effector of 53BP1 and participates in 53BP1-dependent inhibition of end resection. Interestingly, while RIF1 accumulation at DSBs is antagonized by BRCA1 in S and G2 phases, the translocation of BRCA1 to damage sites in G1 cells is inhibited by RIF1, indicating that 53BP1-dependent pathway and BRCA1 counteract each other in a cell cycle-dependent manner. We showed that this cell cycle-dependent regulation is in part regulated by BRCA1-dependent inhibition of 53BP1 phosphorylation in S/G2 phase cells, which requires the E3 ubiquitin ligase activity of BRCA1. Besides RIF1, another DNA damage repair protein PTIP could also act downstream of 53BP1 and counteract BRCA1 function in DNA repair. We discovered that a nuclease SNM1C/Artemis associates with PTIP and functions to prevent end resection and HR repair. In addition, we and others demonstrated that REV7/MAD2L2 acts downstream of RIF1 and inhibits HR repair. Therefore, it is believed that 53BP1 controls RIF1-REV7 and PTIP-Artemis to promote NHEJ and suppress HR repair. We and others recently uncovered another 53BP1-binding protein, NUDT16L1 (also called Tudor Interacting Repair Regulator, TIRR), which associates with 53BP1 and regulates 53BP1 localization to DNA damage sites. We are now further investigating the regulation of DSB repair pathways and damage-induced checkpoint control. In addition, we are performing genome wide CRISPR/Cas9 screens and have identified RNASEH2 deficiency as potential biomarker for ATR inhibitor (ATRi)-based therapy. Moreover, we showed that ATRi could potentiate radiation-induced anti-tumor immune response. Therefore, these studies reveal the interplays between DNA damage repair and multiple cellular processes, which will help improve therapeutic outcome for cancer patients.

Angela K. Eggleston, Ph.D., Senior Editor and Biology Team Leader

Nature

Angela Eggleston received her B.S. in Microbiology and M.S. in Molecular Genetics from the University of Notre Dame, in South Bend, IN. She received her Ph.D. in Biochemistry and Molecular Biology, studying with Steve Kowalczykowski at Northwestern University Medical School in Chicago, IL and at the University of California, Davis. Her doctoral studies concerned the role of the *E. coli* RecBCD helicase/ nuclease in the initiation of genetic recombination and resulted in a U.S. patent. For her postdoctoral studies, she decamped to England and joined Steve West at the Clare Hall Laboratories of the Imperial Cancer Research Fund (now Cancer Research UK). There she studied the opposite end of the recombination process, characterizing the *E. coli* Ruv ABC Holliday junction resolution complex. Her postdoctoral work was sponsored in part by a Burroughs-Wellcome Fund Hitchings-Elion Fellowship. She then undertook a short post-doctoral fellowship with Fred Alt at HHMI/ Children's Hospital in Boston, MA, studying the biochemistry of nonhomologous end joining in mammalian cells. Following this, she entered the realm of scientific publishing, joining Nature Publishing Group in October 1999 as an Associate
Editor for *Nature Cell Biology,* traveling back to London to do so. In July 2001, she moved to Cell Press in Cambridge, MA as a Senior Editor, handling manuscripts for *Cell, Molecular Cell,* and *Developmental Cell* In September 2003, she returned to Nature Publishing Group as a Senior Editor for *Nature.* In 2006, she was promoted to be one of the Biology Team Leaders. She works out of Boston, handling manuscripts on DNA and RNA metabolism and synthetic biology, the biochemistry /biophysics of photosynthesis and motor proteins, bibliometrics, and science policy. In her spare time, she is an avid soccer player, rower, and bonsai student.



Dangsheng Li, Ph.D.
Professor, Shanghai Institute of Biochemistry and Cell Biology, CAS
Deputy Editor-in-chief, *Cell Research*
Executive Editor, *Cell Discovery*
E-mail: dsli@sibs.ac.cn

Dr. Li graduated from USTC (University of Science and Technology of China) in 1988 and obtained his Ph.D. degree from Cornell University Medical College in 1995. He was a postdoctoral fellow at New York University Medical Center from 1996 to 2004. Then he served as an Associate Editor of *Cell* from 2004 to 2006. He has been the Deputy Editor-in-chief of *Cell Research* since 2006. He founded *Cell Discovery* in 2015 and served as its Executive Editor. Dr. Li has co-authored over 50 peer-reviewed papers in journals such as Cell, Cell Host & Microbe, Cell Research, Cell Stem Cell, Developmental Cell, EMBO Journal, Genes & Development, Journal of Biological Chemistry, Molecular and Cellular Biology, Nature Immunology, Science Signaling. Dr. Li has received many awards for his excellent work in publishing, such as National Leading Talent in Publishing in 2008, Tan Jiazhen Award of Life Sciences in 2012, and State Award on Publishing in 2013.

Xin Lu, FMedSci, (Hon) FRCPath, FRSB , PhD, E-mail: xin.lu@ludwig.ox.ac.uk

Professor Xin Lu became the Director of the London Branch of the Ludwig Institute for Cancer Research in 2004 and in 2007 established LICR Oxford. She is the Co-Director of Cancer Research UK Oxford Centre and Lead for Oxford Biomedical Research Centre Cancer Theme. Professor Lu is an elected Member of the European Molecular Biology Organisation (EMBO), Honorary Fellow of the Royal College of Pathologists ((Hon), FRCPath), Fellow of the Royal Society of Biology (FRSB) and Fellow of the Academy of Medical Sciences (FMedSci).

Cellular plasticity, cellular heterogeneity and single cell sequencing

Abstract: Tumour heterogeneity underlies differences in cancer progression and responses to therapy and is caused by genetic and cellular heterogeneity. Cellular heterogeneity is itself caused by cellular plasticity. More than 80% of human tumours originate from epithelial cells, which have the unique property of cell polarity. Cell polarity is a defence against infection and cancer cell invasion. Prof Lu will discuss how epithelial cell plasticity is controlled at several levels: from external signals influencing cell polarity and cell adhesion to gene regulation. She will also illustrate how single cell sequencing can enable us to study cellular heterogeneity in human tissues. Prof Lu's work on epithelial cancers particularly focuses on stomach cancer and oesophageal cancer. Her group is investigating the molecular basis of these cancers and their heterogeneous characteristics, which influence disease risk, diagnosis and responses to therapy. For example, one of the most significant risk factors for oesophageal adenocarcinoma (OAC) is Barrett's oesophagus, a non-malignant chronic inflammatory condition, and identification of those Barrett's oesophagus patients who have a high-risk of progression to OAC would provide important opportunities for intervention and prevention. Prof Lu's group is taking a single cell genomics approach to investigate the pre-malignant lesions and how cancer-initiating cells arise.

Cellular plasticity, cellular heterogeneity and single cell sequencing

Tumour heterogeneity underlies differences in cancer progression and responses to therapy and is caused by genetic and cellular heterogeneity. Cellular heterogeneity is itself caused by cellular plasticity. More than 80% of human tumours originate from epithelial cells, which have the unique property of cell polarity. Cell polarity is a defence against infection and cancer cell invasion. Prof Lu will discuss how epithelial cell plasticity is controlled at several levels: from external signals influencing cell polarity and cell adhesion to gene regulation. She will also illustrate how single cell sequencing can enable us to study cellular heterogeneity in human tissues. Prof Lu's work on epithelial cancers particularly focuses on stomach cancer and oesophageal cancer. Her group is investigating the molecular basis of these cancers and their heterogeneous characteristics, which influence disease risk, diagnosis and responses to therapy. For example, one of the most significant risk factors for oesophageal adenocarcinoma (OAC) is Barrett's oesophagus, a non-malignant chronic inflammatory condition, and identification of those Barrett's oesophagus patients who have a high-risk of progression to OAC would provide important opportunities for intervention and prevention. Prof Lu's group is taking a single cell genomics approach to investigate the pre-malignant lesions and how cancer-initiating cells arise.

Feng Shao, Ph.D.
Investigator and Deputy Director
National Institute of Biological Sciences (NIBS) Beijing, China

Dr. Feng Shao was a chemistry undergraduate of Peking University (1991-1996) and obtained his PhD with Dr. Jack E. Dixon from University of Michigan (with a Distinguished Dissertation Award) in 2003. Prior to returning to China in 2005 to assume an assistant investigator at NIBS, he was a Damon Runyon Postdoc Research Fellow at Harvard Medical School. Dr. Shao was promoted to become an associate investigator in 2009 and a full investigator in 2012 at NIBS.

Dr. Shao's research spans from bacterial pathogenesis to innate immunity and to pyroptotic cell death. His group has identified several cytosolic innate immune pattern recognition receptors, including the NAIPs for bacterial flagellin and Pyrin for Rho-modifying bacterial toxins in the caspase-1 inflammasome pathway, caspase-11/4/5 for cytosolic LPS as well as ALPK1 for ADP-heptose (a precursor for LPS biosynthesis). He has also identified Gasdermin-D (GSDMD) whose cleavage by caspase-1/4/5/11 determines pyroptosis, critical for innate defense and sepsis. Dr. Shao's research further establishes a Gasdermin family of pore-forming factors, thereby re-defining pyroptosis as Gasdermin-mediated programmed necrosis. Among the family, Gasdermin-E (GSDME) is activated by caspase-3, which has important contributions to the adverse effect of chemotherapy drugs.

Dr. Shao's work has been well recognized by numerous prestigious awards including the HHMI International Early Career Award (2012), The CBIS Young Investigator Award (2013), the Irving Sigal Young Investigator Award from the Protein Society (2013), The Wu Jieping-Paul Janssen Medical & Pharmaceutical Award (2014), The Ho Leung Ho Lee Foundation Award for Science & Technology Progress (2016) and the SCBA Kenneth Fong Young Investigator Award (2017). He is an elected member of the Chinese Academy of Science (2015), an associate member of European Molecular Biology Organization (EMBO) (2015), and a fellow of American Academy of Microbiology (2016).

Innate sensing of cytosolic LPS: pyroptosis and beyond

Lipopolysaccharide (LPS), the major cell-wall component of Gram-negative bacteria, is long known to be sensed by the plasma membrane-bound TLR4 receptor. Ligation of TLR4 by the lipid A of LPS stimulates NF-κB and IRF-mediated inflammatory cytokine production. Recently, we showed that caspase-11, 4 and 5 are cytosolic immune receptors for LPS and activated by direct binding to its lipid A part. Like caspase-1 activation by the canonical inflammasome, caspase-11/4/5 activation induces pyroptosis, both of which are critical for antibacterial defense and development of immunological diseases. Caspase-11/4/5 and caspase-1 cleave Gasdermin D (GSDMD) to release the autoinhibition of its N-terminal domain that bears an intrinsic pore-forming activity for executing pyroptotic cell death. *Gsdmd*$^{-/-}$ mice are susceptible to various bacterial infections and also resist LPS-induced septic shock. GSDMD belongs to a large Gasdermin family sharing the pore-forming domain. Another family member GSDME whose expression is silenced in most cancer cells, is activated by caspase-3 cleavage; inflammatory damages caused by GSDME-mediated pyroptosis is the major determinant for the toxicity of those DNA-damaging chemotherapy drugs. Lastly, we discover that ADP-heptose, the precursor for LPS inner core oligosaccharide, is recognized in host cytosol by a novel kinase receptor ALPK1. Like lipid A-activated TLR4, ADP-heptose-activated ALPK1 potently stimulates NF-κB-dependent inflammatory responses both in cells and mice. These findings shift the paradigm of immune sensing of LPS and antibacterial defense, and open several new areas of research on innate immunity and pyroptosis-mediated inflammation. The cell-entry property of ADP-heptose also suggests a new way of modulating immune responses in mammals.

Lee Zou, PhD

Professor, Harvard Medical School

Associate Scientific Director, MGH Cancer Center

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Education:

- B.S. (1992), Sun Yat-Sen (Zhongshan) University
- M.S. (1994), Kansas State University
- PhD (1999), Stony Brook University & Cold Spring Harbor Laboratory
- Postdoc (2000-2003), Baylor College of Medicine
- Postdoc (2003-2004), Harvard Medical School

Other Positions:

- Editorial Board: Molecular Cell, MCB, JBC, Cancer Res.

Research Interests:

- DNA damage signaling, DNA replication, cancer therapy

Representative Publications:

•Kabeche, L., Nguyen, H. D., Buisson, R., and **Zou, L.** (2018) A mitosis-specific and R loop-driven ATR pathway promotes faithful chromosome segregation. ***Science*** 359:108-114.

•Nguyen, H. D., Yadav, T., Giri, S., Saez, B., Graubert, T. A., and **Zou, L.** (2017) Functions of RPA as a Sensor of R Loops and a Regulator of RNaseH1. ***Mol. Cell*** 65:832-847.

•Buisson, R., Joshi, N., Rodrigue, A., Ho, C. K., Kreuzer, J., Foo, T. K., Hardy, E., Dellaire, G., Hass, W., Xia, B., Masson, J. and **Zou, L.** (2017) Coupling of Homologous Recombination and the Checkpoint by ATR. ***Mol. Cell*** 65:336-346.

•Flynn, R. L., Cox, K. E., Jeitany, M., Wakimoto, H., Bryll, A. R., Ganem, N. J., Bersani, F., Pineda, J. R., Suva, M., Benes, C. H., Haber, D. A., Boussin, F. D., and **Zou, L.** (2015) Alternative Lengthening of Telomeres Renders Cancer Cells Hypersensitive to ATR Inhibitors. ***Science*** 347:273-277.

•Flynn, R. L., Centore, C. R., O'Sullivan, R. J., Rai, R., Tse, A., Songyang, Z., Chang, S., Karlseder, J., and **Zou, L.** (2011) TERRA and hnRNPA1 Orchestrate an RPA-to-POT1 Switch on Telomeric Single-Stranded DNA. ***Nature*** 471:532-536.

The ATR Signaling Circuitry: from Basic Research to Targeted Cancer Therapy

ATR is a master regulator of cellular responses to DNA replication stress. To understand how ATR responds to replication stress in cancer cells, we sought to identify the specific types of oncogenic events that activate ATR. APOBEC3A/B are members of the APOBEC family of cytidine deaminases. The mutation signatures associated with APOBEC3A/B are readily detected in a number of cancer types, suggesting that APOBEC3A/B are key drivers of mutations in the cancer genome. We found that APOBEC3A/B activity imposes replication stress and activates ATR in cancer cells. The ability of APOBEC to generate replication stress relies on cytidine deamination and abasic site formation at replication forks. APOBEC-induced abasic sites promote single-stranded DNA (ssDNA) accumulation and ATR activation. When ATR is inhibited, ssDNA continues to accumulate in the presence of APOBEC activity, driving cells into replication catastrophe. These results demonstrate that ATR plays a key role in restricting the APOBEC-induced ssDNA in cancer cells, suggesting that ATR is a potential therapeutic target in cancer cells harboring high APOBEC3A/B activity.

In addition to the replication stress induced by APOBECs, we also investigated the distribution of APOBEC-induced mutations in the cancer genome. We found that the APOBEC-associated mutation signature is significantly enriched in DNA hairpins in tumors. Among the APOBECs implicated in the mutagenesis in tumors, APOBEC3A is the only one displaying a clear preference for substrate sites in DNA hairpins in vitro. Importantly, the structural preference of APOBEC signature mutations in tumors perfectly matches the structural preference of APOBEC3A in vitro, strongly suggesting that APOBEC3A is the main driver of these hairpin mutations in the cancer genome. Furthermore, many APOBEC3A-induced mutations are recurrent outside of known driver genes in tumors, revealing an unexpected class of recurrent cancer mutations that arise independently of functional selection. Thus, our results suggest that recurrent cancer mutations are not only generated by functional selection, but also by oncogenic mutation drivers with sequence and structural preferences, providing a new angle for the analysis of recurrent mutations in tumors.

Hongtao Yu, Ph.D.

Professor, Department of Pharmacology
Investigator, Howard Hughes Medical Institute
Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology
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Hongtao Yu is Professor of Pharmacology at the University of Texas (UT) Southwestern Medical Center at Dallas and Investigator at the Howard Hughes Medical Institute (HHMI). Dr. Yu was born in China in 1969. He received his B.S. in Chemistry from Peking University(Beijing, China) in 1990. He went to the United States to pursue his graduate studies, and received his Ph.D. in Chemistry from Harvard University (Cambridge, MA) in 1995. His thesis research with Dr. Stuart Schreiber focused on the structure determinat ion of protein modules in signal transduction by nuclear magnetic resonance (NMR) spectroscopy. He then completed his postdoctoral training (1995-1999) with Dr. Marc Kirschner at Harvard Medical School(Boston, MA). During his postdoctoral training, Dr. Yu studied the composition, function, and regulation of the anaphase -promoting complex or cyclosome (APC/C), a multisubunit ubiquitin ligase critical for cell cycle progression. Dr. Yu began his independent research career in 1999 in the Department of Pha rmacology at UT Southwestern Medical Center, and was promoted to Associate Professor with tenure in 2004 and to Professor in 2008. He was selected as an HHMI Investigator in 2008, and was elected a Fellow of the American Association for the Advancement of Science (AAAS) in 2012. Using a multidisciplinary approach, his lab has contributed significantly to our molecular understanding of chromosome segregation and genome maintenance.

Mitotic Checkpoint Regulators in Chromosome Segregation and Insulin Signaling

The long-term goal of my research program is to understand chromosome segregation at a deep, mechanistic level. A major focus of my lab is the spindle checkpoint, which ensures accurate chromosome segregation during mitosis and suppresses aneuploidy and its associated dire consequences, such as cancer and birth defects. Kinetochores not properly attached to the mitotic spindle recruit and activate spindle checkpoint proteins to delay anaphase onset. Our recent studies have defined a conserved mechanism for sensing unattached kinetochores. We have successfully reconstituted downstream events of spindle checkpoint signaling in the test tube. We have discovered an unexpected connection between the spindle checkpoint proteins and insulin signaling. Specifically, a checkpoint module directly binds to the insulin receptor and regulates its endocytosis. We have further identified a feedback regulatory mechanism that controls insulin receptor endocytosis. Targeting this feedback regulation prolongs insulin action at the plasma membrane and alleviates high-fat-diet-induced diabetes in mice. Our findings provide a clear example of evolutionary repurposing and reveal intimate crosstalk between the spindle checkpoint and insulin signaling.

Concurrent Session Abstracts (Sorted by Sessions)

Concurrent Session 1: Signaling in Diseases

Xiaodong Chen – The University of Texas Health Science Center
Exchange proteins directly activated by cAMP as major therapeutic targets
The pleotropic second messenger cAMP is an important stress signal that regulates a multitude of physiological functions under normal and diseased conditions. The major cellular effects of cAMP are transduced by two ubiquitously expressed intracellular cAMP receptors, protein kinase A (PKA) and exchange protein directly activated by cAMP (EPAC) in human. Using genetically engineered EPAC knockout mouse models, we have demonstrated that EPAC proteins play important roles in the development of major human diseases, including obesity, cancer and chronic pain etc. Furthermore, we have developed first-in-class EPAC specific inhibitors with favorable in vivo pharmacological and toxicological profiles. Applications of EPAC inhibitors in various animal disease models related to chronic pain and cardiovascular diseases recapitulate the genetic phenotypes of EPAC knockout mice. These Studies validate the therapeutic potentials of small molecule EPAC specific inhibitors.

Xin-Hua Feng – Zhejiang University
Loss of TGF-beta Cytostatic Signaling in Cancer
Loss of the antiproliferative response is a hallmark in human cancers. Tumor cells have developed a number of strategies to escape from negative growth control. One major mechanism to resist the cytostatic effect of anti-growth factor such as TGF-□ is through inactivating mutations/deletions in the TGF-□ signaling pathway, which frequently occur in gastrointestinal and pancreatic cancer. For example, tumor suppressor Smad4/DPC4, the central transducer of TGF-□ signaling, is deleted in more than half of pancreatic cancer patients. However, deletion or mutations in the Smad4 gene are rare in other types of cancers. We have taken functional genomic, proteomic and cell biological approaches to study how the tumor suppressor function is regulated in normal and cancer cells. We found that activation of many oncoproteins can cause TGF-□ resistance. Our novel studies gain conceptual insights into the oncoprotein-tumor suppressor interplay in tumorigenesis and provide guidance to logical therapeutic designs in cancer prevention, diagnostics and treatment.

Kun-Liang Guan – University of California San Diego
Regulation of the Hippo tumor suppressor pathway
The Hippo pathway is crucial in organ size control and its dysregulation contributes to tumorigenesis. Core components of the Hippo pathway include the protein kinases of MST1/2, MAP4Ks, LATS1/2, the transcription co-activators YAP/TAZ and their DNA binding partners TEADs. LATS phosphorylates YAP/TAZ to promote cytoplasmic localization and degradation, thereby inhibiting YAP/TAZ and cell growth. The Hippo pathway is regulated by a wide range of signals, including cell density, GPCR, cellular energy levels, and mechanical cues. We recently discovered that TEAD shuttles to cytoplasm in a Hippo independent manner. Moreover, we have elucidated a molecular mechanism of Hippo pathway regulation by matrix stiffness and a critical role of Rap2 in mechano transduction. The emerging role of the Hippo pathway in tumorigenesis suggests potential therapeutic value of targeting this pathway for cancer treatment.

Xuelian Luo –UT Southwestern Medical Center
The STRIPAK PP2A complex couples upstream inputs to control Hippo kinase activation
The Hippo pathway is a growth control pathway that plays key roles in organ size control, tissue homeostasis and tumor suppression. The mammalian Hippo pathway contains a core MST-LATS kinase cascade. Recently, we have shown that the STRIPAK PP2A complex is a

key negative regulator of Hippo signaling in human cells. MST2 interacts with STRIPAK through the adaptor protein SLMAP. The SLMAP-containing STRIPAK complex specifically blocks MST2 activation by dephosphorylating phospho-T180 (pT180) at its activation loop. Inactivation of STRIPAK-SLMAP leads to spontaneous activation of the Hippo pathway without upstream signals. In our most recent studies, we have defined the core components of the specific STRIPAK complex critical for MST2 inhibition in human cells. We have shown that the FERM-domain proteins promote SAV1-mediated inhibition of PP2A A-C in vitro. Conversely, phosphorylation of SAV1 by the GCK-III kinase blocks STRIPAK-mediated inhibition of MST2. Therefore, STRIPAK serves as a major signaling platform that enables the regulation of MST2 activation by upstream regulators.

Cun-Yu Wang – University of California Los Angeles

Metabolic Control of Adult Stem Cell Fate and Bone-Fat Balance in Aging

Mesenchymal stem/stromal cells (MSCs) or skeletal stem cells are adult stem cells in bone marrow. Abnormal lineage commitment of mesenchymal stem/stromal cells (MSCs) contributes to the reduced bone mass and increased marrow adipose tissue (MAT) in osteoporosis and skeletal aging. Although master regulators that control bone and fat cell lineages have been identified, little is known about factors that are associated with MAT accumulation and osteoporotic bone loss. We identify peroxisome proliferator-activated receptor γ coactivators 1-α (PGC-1α) as a critical switch of cell fate decision, whose expression decreased with aging in MSCs. Unexpectedly, loss of PGC-1α promoted adipogenic differentiation of MSCs at the expense of osteoblastic differentiation. Conditional deletion of PGC-1α in MSCs impaired bone formation while enhancing MAT accumulation in osteoporosis. Conversely, induction of PGC-1α attenuated osteoporotic bone loss and MAT accumulation. Mechanistically, PGC-1α was found to maintain bone and fat balance by inducing the transcription factor TAZ. Taken together, our results provide critical insights into bone-fat imbalance in osteoporosis, suggesting that PGC-1α is an important therapeutic target in treatments for osteoporosis and skeletal aging.

Concurrent Session 2: Neural Circuit and Development

Yulong Li – School of Life Sciences, Peking University
Identification of Human MRGPRX4 as A Novel Bile Acid Receptor for Chronic Itch
Patients with liver diseases often suffer from cholestatic pruritus, severe and chronic itching of the skin. Identification of the pruritogen(s) and their corresponding receptor(s) in human would be the key to develop effective treatments. Here we identified bile acids and mas-related GPCR member X4 (MRGPRX4) as the pruritogen and receptor for cholestatic pruritus respectively. The orphan GPCR receptor MRGPRX4 was expressed in a subset of itch-related dorsal root ganglia (DRG) neurons and potently activated by human endogenous bile acids. Application of bile acids elicited a robust calcium response in human DRG neurons and caused pruritus in healthy human subjects. More strikingly, elevated levels of plasma bile acids were detected in patients with cholestatic pruritus, sufficient to activate MRGPRX4. Taken together, our work discovered human ligand and receptor responsible for cholestatic pruritus and identified MRGPRX4 as a promising drug target for cholestatic pruritus treatment.

Xiangmin Xu – University of California, Irvine
New Hippocampal Circuit Organization and Function
New advances in virology and genetic technology offer powerful tools for studies of neural circuit organization and function. In this talk, Dr. Xu will highlight his lab's applications of viral genetic tools in mapping hippocampal neural circuits related to spatial learning and memory. He will discuss insights from their studies of the larger cortico-hippocampal circuitry associated with subiculum (SUB) projections to CA1 using the latest technologies of neuroscience. Specifically, their recent work identified a distinct sub-population of SUB neurons forming a pathway from visual cortex to CA1 and perirhinal cortex, and demonstrates that this pathway plays a critical role in object-place learning.

Fuqiang Xu – Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences
Virus-based tools for neurocircuit studies
All our brain functions, such as basic condition-controlling, learning, decision-making, are based on corresponding neuronal circuits, and accordingly, "Mental illness is defined as disruption in neural circuits". For a complete elucidation of the mechanisms of a given brain function or disease, we must know the exact structures of all circuits related to that function precisely. However, the studies at circuit level on both structures and functions have been hindered by lacking of effective tools. In the past decade, the group has been developing tools for structural and functional studies of neuronal circuits, and mostly through collaborations, to apply the tools to reveal the detailed structures of neuronal connections, and the corresponding functions and properties. By integrating the principles and recent developments from the related fields, hundreds of virus-based tools have been successfully established and further used by hundreds of laboratories and hospitals for a variety of purposes. I will give a brief introduction on the arsenal and an update of the progresses in our laboratory on the relevant topics.

Guoqiang Bi – University of Science and Technology of China, Hefei, China
Multiscale imaging of neuronal synapses and circuits
The complex brain functions such as perception, learning and emotion arise from its intricate structures: from the synapse that operates as the basic unit of information processing and storage to the network of neuronal circuits across the whole brain. In this talk, I will share our recent work in the development and application of new imaging techniques to visualize brain structures of various length scales, including correlative light-electron microscopy and cryo electron tomography for ultrastructural study of identified neuronal synapses in their native states, as well as ultra-high speed volumetric fluorescence microscopy to map the structure and activity trace in rodent and primate brains.

Hongwei Dong, University of Southern California
Assembling global neural networks of the mouse brain
The longterm objective of the Mouse Connectome Project at USC (MCP; www.MouseConnectome.org) is to map the interconnections among all regions of the C57Bl/6 mouse brain, to generate a corresponding comprehensive connectome map that represents the interconnections in a common neuroanatomic frame, and to understand how the di¬fferent brain regions assemble into functional networks based on these connections. The biological significance of assembling a brain-wide wiring diagram is tantamount to that of the Human Genome Project. However, just as knowing the sequence of three billion base pairs in the human genome reveals little about how our bodies are regulated by genes, constructing the connectome will not directly reveal its functional purpose. The ensuing challenge is to analyze the vast connectivity information in a way that is most conducive to generating novel behavioral hypotheses for experimental testing.As a part of the NIH BRAIN Initiative (https://www.braininitiative.nih.gov/), our Mouse Connectome Project has made significant progress over the last 7 years. We have generated the first and the most comprehensive connectomic map of the cerebral cortex available for any mammalian species (Zingg et al., Cell, 2014). Computational analysis of this map revealed that the mammalian cerebral cortex, long thought to be a dense single interrelated tangle of neural networks, was composed of relatively few functionally segregated cortico-cortical subnetworks. Subsequently, we also constructed (1) a comprehensive mesoscale mouse cortico-striatal projectome (Hintiryan et al., Nature Neuroscience, 2016), which is a detailed connectivity projection map from the entire cerebral cortex to the dorsal striatum or caudoputamen in rodents; (2) the genetic architecture and wiring diagram of the mouse hippocampus (Bienkowski et al., Nature Neuroscience, 2018), which I will elaborate in more detail in my talk. Following the same principle and strategy, we project to systematically and comprehensively assemble the global neural networks and a Google earth-like map of the entire mouse brain within the next 5-10 years.

Tian Xue – University of Science and Technology of China
Intrinsic photosensitive retinal ganglion cells mediate light facilitated cross-modal cortical development
Sensory experiences drive neuronal plasticity and forge the development of sensory cortices. Early experience of one sensory modality stimulates the axonal growth, dendritic branching and synaptogenesis in the correspondent sensory cortices and also in cortices associated with other sensory modalities. Among all the sensory modalities, visual experiences appear only after the opening of the eyes. However, light sensation starts early at the embryonic stage carried by intrinsic photosensitive retinal ganglion cells (ipRGCs). In rodents, ipRGCs mediate the only light sensation until the postnatal day 10 and the neonatal cell density of ipRGCs is 5 times higher than that in the adult retina. This early light sensation has been implicated to drive the development of non-image-forming brain areas. Surprisingly, we showed ipRGCs mediated early light sensation was both necessary and sufficient for the early development of multiple cortices of mice. We uncovered a brand-new function of ipRGCs and enriched the reservoir of non-image-forming functions. Our work highlighted the importance of light sensation on the development before the visual experiences.

Concurrent Session 3: DNA and RNA Modification

Yungui Yang – Beijing Institute of Genomics
Gene Regulations Mediated by RNA Modifications
Over 100 types of chemical modifications have been identified in various types of RNAs including non-coding RNA and mRNA, among which methylation is the most common modification. The N6- methyl-adenosine (m6A) and N5-methyl-cytosine (m5C) are the most common and abundant internal modifications on mRNA molecules. The recent identification of methyltransferases METTL3/METTL14/WTAP and NSUN2, and m6A demethylases ALKBH5 and FTO, supports the reversibility of RNA methylation. Several YTH-domain-containing proteins YTHDF1-3 and YTHDC1-2 specifically binding to m6A and ALYREF recognizing m5C have been identified to regulate various mRNA processing, suggesting vital roles of RNA modifications in gene expression control. Our recent works revealed indispensable roles of m6A in mRNA translation, spermatogonial differentiation, and haematopoietic stem and progenitor cell specification, and 5-methylcytosine promotes mRNA export. We have further performed RNA-BisSeq to map transcriptomic profiles of m5C in early embryos of Zebra fish and human cancers. We will discuss the recent progress in RNA modifications and their potential biological significance in this conference.

Jianjun Chen – Beckman Research Institute of City of Hope
The Role and Therapeutic Implication of RNA Modification in Cancer
N6-methyladenosine (m6A), the most abundant internal modification in eukaryotic mRNAs, has been shown to play essential roles in various normal bioprocesses. Evidence is emerging that m6A modification and the associated regulatory proteins also play critical roles in cancer. We have revealed the important functions of m6A regulatory proteins (e.g., FTO and METTL14) in cancer, especially acute myeloid leukemia (AML), and have developed novel therapeutic strategies based on such discoveries to treat leukemia.
Briefly, we found that FTO is highly expressed in certain subtypes of AMLs including AMLs carrying t(11q23), t(15;17), NPM1 mutation, and/or FLT3-ITD, in which FTO plays an essential oncogenic role in promoting leukemogenesis and in affecting drug response through post-transcriptionally regulating expression of its critical target RNAs (such as ASB2 and RARA) in an m6A-dependent manner. Subsequently, we found that FTO is also a direct target of R-2-hydroxyglutarate (R-2HG), which is produced at high levels by mutant isocitrate dehydrogenase 1/2 (IDH1/2) enzymes and has been reported as an oncometabolite. We show that by inhibiting FTO activity, which in turn leads to increased global m6A modification in leukemia cells, R-2HG exhibits a broad and intrinsic anti-tumor effect in vitro and in vivo. High levels of FTO sensitize leukemic cells to R-2HG. Thus, while R-2HG accumulated in IDH1/2-mutant cancers contributes to cancer initiation, our work demonstrates broad anti-tumor effects of 2HG in inhibiting proliferation of FTO-high cancer cells. We also show that METTL14 is overexpressed in AML and plays a critical role in the development and drug response of AML, and is also required for the self-renewal of leukemia stem cells, by post-transcriptionally regulating of expression of a set of essential oncogenes such as MYC and MYB. Very recently, we have developed highly selective and effective FTO inhibitor compounds that shows potent therapeutic effects in treating human AML in preclinical animal models, demonstrating that as an mRNA demethylase, FTO is a druggable target for AML treatment.
Taken together, our studies highlight the critical roles and therapeutic implictaion of m6A modification and its regulatory proteins in cancer (e.g., leukemia).

Hongjun Song –Perelman School of Medicine at the University of Pennsylvania
Epitranscriptomic regulation in the mammalian nervous system
N^6-methyladenosine (m^6A), installed by the Mettl3/Mettl14 methyltransferase complex, is the most prevalent internal mRNA modification. The functional role of m^6A signaling in the nervous system is not well understood. We used both in vivo mouse model and in vitro human iPSC-derived 2D and 3D brain organoid models. We found that m^6A depletion by

Mettl14 knockout in embryonic mouse brains prolongs the cell cycle of radial glia cells and extends cortical neurogenesis into postnatal stages. m^{6}A depletion by Mettl3 knockdown also leads to a prolonged cell cycle and maintenance of radial glia cells in mice. m^{6}A sequencing of embryonic mouse cortex shows enrichment of mRNAs related to transcription factors, neurogenesis, the cell cycle, and neuronal differentiation, and m^{6}A tagging promotes their decay. Further analysis uncovers previously unappreciated transcriptional pre-patterning in cortical neural stem cells. Similarly, m^{6}A signaling regulates human cortical neurogenesis in forebrain organoids via regulation of cell cycle progression. Comparison of m^{6}A-mRNA landscapes between mouse and human cortical neurogenesis reveals enrichment of human-specific m^{6}A tagging of transcripts related to brain-disorder risk genes (Yoon et al. *Cell* 2017). In the mature nervous system, m^{6}A-seq shows a dynamic but distinct landscape of m^{6}A-tagged transcriptomes and m^{6}A tagging promotes stimulation induced protein translation. We found that axonal injury leads to dynamic changes of m^{6}A dynamics in dorsal root ganglion neurons and m^{6}A signaling is required for injury-induced protein translation of regeneration-associated genes and functional axonal regeneration. Our studies suggest developmental stage- and cell type-specific epitranscriptomic modification of transcriptomes and functions in the mammalian nervous systems.

Linheng Li –Stowers Institute for Medical Research

Expanding human blood-forming stem cells via manipulating the M6A pathway

Transplantation of hematopoietic stem cells (HSCs) from human umbilical cord blood (hUCB) holds great promise for treating a broad spectrum of hematological disorders including cancer, but the limited number of HSCs in a single hUCB unit restricts its widespread use. Although extensive efforts have developed multiple methods for ex vivo expansion of human HSCs by targeting single molecules or pathways, it remains unknown whether simultaneously manipulating a large number of targets essential for stem cell self-renewal could be achievable. Recent studies have emerged that N6-methyladenosine (m6A) modulates expression of a group of mRNAs critical for stem cell fate determination by influencing their stability. Among several m6A readers, Ythdf2 is well recognized to promote the targeted mRNA decay. However, the physiological functions of Ythdf2 on adult stem cells are still elusive. Here we show that conditional knockout (KO) mouse Ythdf2 increased phenotypic and functional HSC numbers, but neither skewed lineage differentiation nor led to hematopoietic malignancies. Furthermore, knockdown (KD) of human YTHDF2 led to over 10-fold increase in ex vivo expansion of hUCB HSCs, 5-fold increase in colony-forming units (CFUs), and more than 8-fold increase in functional hUCB HSCs in the secondary serial of limiting dilution transplantation assay. Mechanistically, m6A mapping of RNAs from mouse hematopoietic stem and progenitor cells (HSPCs) as well as from hUCB HSCs revealed m6A enrichment on mRNAs encoding transcription factors critical for stem cell self-renewal. These m6A-marked mRNAs were recognized by Ythdf2 and underwent mRNA decay. In Ythdf2 KO HSPCs and YTHDF2 KD hUCB HSCs, these mRNAs were stabilized, leading to an increase in protein levels and facilitating HSC expansion. Knockdown one of the Ythdf2 key targets, Tal1 mRNA, partially rescued the phenotype. Therefore, our study for the first time shows the function of Ythdf2 in adult stem cell maintenance and identifies an important role of Ythdf2 in regulating HSC ex vivo expansion via the mechanism of controlling the stability of multiple mRNAs critical for HSC self-renewal, thus having a strong potential for future clinical applications.

Housheng Hansen He –Princess Margaret Cancer Center/University Health Network

m^{6}A epitranscriptome profiling in patient tumors

N6-Methyladenosine (m6A) accounts for 0.2~0.6% of all adenosine in mammalian mRNA, representing the most abundant internal mRNA modification. m6A RNA immunoprecipitation followed by high-throughput sequencing (MeRIP-seq) is a powerful technique to map the m6A location transcriptome-wide. However, this method typically requires large amount of total RNA, which limits its application to patient tumours. We optimized a few key parameters and with a refined m6A MeRIP-seq protocol we were able to profile the m6A

epitranscriptome using as low as 500 ng of total RNA from patient tumours. Through integrative analysis of the transcriptome, m6A epitranscriptome and proteome data in 50 lung cancer patient tumours, we identified dynamics at the m6A level that account for the discordance between mRNA and protein levels in these tumours.

Chengqi Yi – Peking University

Chemical-assisted sequencing of DNA and RNA modifications

Modified nucleotides, especially those related to epigenetic or epitranscriptomic functions, provide critical regulatory information beyond their sequence and also define cell status in higher organisms. The discovery of these modified nucleotides has triggered an explosion of new information in the fields of DNA/RNA epigenetics. This rapid research progress has benefited significantly from timely developments of high-throughput sequencing technologies that enable identifications of these nucleotide modifications in the whole genome or transcriptome. In my laboratory, we utilize selective chemical labeling to develop high-resolution sequencing methods for these modified nucleotides; in particular, we have developed several technologies for the genome/transcriptome-wide sequencing of 5-hydroxymethylcytosine (5hmC), 5-formylcytosine (5fC) and deoxyuridine (dU) in DNA, and pseudouridine (Ψ) and 1-methyladenosine (m1A) in RNA, respectively; such chemical labeling-enabled sequencing technologies will allow future functional studies of these modified nucleotides.

Concurrent Session 4: Metabolism and Cancer

Zhimin Lu - MD Anderson Cancer Center
Metabolic Feature of Cancer Cells
Cancer cells uniquely reprogram their cellular activities to support their rapid proliferation and migration and to counteract metabolic and genotoxic stress during cancer progression. In this reprograming, cancer cells' metabolism and other cellular activities are integrated and mutually regulated, and cancer cells modulate metabolic enzymes spatially and temporally so that these enzymes not only have altered metabolic activities but also have modulated subcellular localization and gain non-canonical functions. We discovered metabolism enzymes' newly acquired functions and the non-canonical functions of some metabolites as features of cancer cell metabolism, which play critical roles in various cellular activities, including gene expression, anabolism, catabolism, redox homeostasis, and DNA repair.

Baoliang Song - Wuhan University
Exploring the regulatory mechanism of cholesterol homeostasis
A high concentration of low-density lipoprotein cholesterol (LDL-C) is a major risk factor for cardiovascular disease. Although LDL-C levels vary among humans and are heritable, the genetic factors affecting LDL-C are not fully characterized. We identified a rare frameshift variant in the *LIMA1* (also known as *EPLIN* or *SREBP3*) gene from a Chinese family of Kazakh ethnicity with inherited low LDL-C and reduced cholesterol absorption. In a mouse model, LIMA1 was mainly expressed in the small intestine and localized on the brush border membrane. LIMA1 bridged NPC1L1, an essential protein for cholesterol absorption, to a transportation complex containing myosin Vb and facilitated cholesterol uptake. Similar to the human phenotype, *Lima1*-deficient mice displayed reduced cholesterol absorption and were resistant to diet-induced hypercholesterolemia. Through our study of both mice and humans, we identify LIMA1 as a key protein regulating intestinal cholesterol absorption.

Wei Xu - University of Wisconsin-Madison
Central roles of PKM2 in the regulation of glucose and lipid metabolism
Metabolic reprogramming is a hallmark of cancer. We discover that the key glycolytic enzyme pyruvate kinase M2 isoform (PKM2), but not the related isoform PKM1, is methylated by co-activator-associated arginine methyltransferase 1 (CARM1). PKM2 methylation reversibly shifts the balance of metabolism from oxidative phosphorylation to aerobic glycolysis in breast cancer cells. Oxidative phosphorylation depends on mitochondrial calcium concentration, which become critical for cancer cell survival when PKM2 methylation in blocked. By interacting with and suppressing the expression of inositol-1,4,5-triphosphate receptors ($InsP_3R_s$), methylated PKM2 inhibits the influx of calcium from endoplasmic reticulum to mitochondria. Therefore, inhibiting PKM2 methylation generates metabolic vulnerability to $InsP_3R$-dependent mitochondrial functions. Our recent genomic and proteomics analyses of PKM2 wild type and knockout (KO) cell lines reveal the essential role of PKM2 in cholesterol synthesis (i.e., cholesterol biosynthesis pathway was significantly decreased in PKM2 KO cells). While the long chain fatty acid and lipid droplets were dramatically decreased in PKM2 KO cells, the free cholesterol remain unchanged, suggesting that PKM2 regulates lipid synthesis. This new finding underscores the broad impact of PKM2 on cancer metabolism by harmonizing both glucose and lipid metabolism. The potential mechanism of PKM2 in regulating the lipid synthesis will be discussed.
Reference:
Liu, F. *et al.* PKM2 methylation by CARM1 activates aerobic glycolysis to promote tumorigenesis. *Nat Cell Biol* **19**, 1358-1370, doi:10.1038/ncb3630 (2017).

Yiguo Wang - Tsinghua-Peking Joint Center for Life Sciences, School of Life Sciences, Tsinghua University, Beijing 100084, China
Hormonal regulation of hepatic glucose metabolism
Hepatic glucose is tightly regulated by hormonal and nutritional signals. Dysfunction of

regulatory signals and glucose metabolism is linked to metabolic diseases such as type 2 diabetes. Here we show that hormonal signaling orchestrate glucose metabolism in the liver during fasting.

Deliang Guo - Ohio State University
Lipid metabolism reprogramming in malignancy, from *de novo* synthesis to storage
Lipid metabolism reprogramming emerges as a new hallmark of malignancy. Highly elevated lipid synthesis and uptake occurs in various types of cancers, while the molecular mechanisms underlying these upregulations remain unclear. We recently identified that sterol regulatory element-binding protein-1 (SREBP-1), a master transcription factor playing a central role in lipid synthesis and uptake, is highly upregulated in malignant brain tumors and mediates oncogenic EGFR signaling to lipid metabolism activation. We found that *N*-glycosylation activates the key transporter SREBP cleavage-activating protein (SCAP) to promote SREBP trafficking and activation, unveiling a molecular link between glucose metabolism and *de novo* lipid synthesis. Interestingly, our recent data show that excess lipids are stored in lipid droplets in malignant brain tumors, which is inversely correlated with patient survival. Blocking lipid storage induces severe oxidative stress that kills tumor cells, suggesting that lipid droplet storage protects tumor cells against potential lipotoxicity induced by excess lipids. Together, our studies demonstrate that SCAP/SREBP-1 activation plays a key role in lipid metabolism upregulation in malignancy, and also provide promising metabolic targets and novel anti-lipid strategy for cancer therapy.

Wei Qi – Shanghai Tech University
Targeting cancer epigenome through PRC2 inhibitor
Polycomb repressive complex 2 (PRC2) consists of three core subunits, EZH2, EED and SUZ12, and plays pivotal roles in transcriptional regulation. The catalytic subunit EZH2 methylates histone H3 lysine 27 (H3K27), and its activity is further enhanced by the binding of EED to trimethylated H3K27 (H3K27me3). Somatic gain-of-function (GOF) mutations of *Ezh2*, which correlates with enhanced PRC2 activity and cause high H3K27me3, have been identified in multiple cancers including follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL). We have previously discovered small-molecule PRC2 inhibitors. One class of these PRC2 inhibitors competes with the cofactor S-adenosylmethionine (SAM), and the other class, such as EED226, directly binds to the H3K27me3 binding pocket of EED. EED226 induces a conformational change upon binding EED, leading to loss of PRC2 activity. EED226 shows similar activity to SAM-competitive inhibitors in blocking H3K27 methylation of PRC2 target genes and inducing regression of human lymphoma xenograft tumors. Interestingly, EED226 also effectively inhibits PRC2 containing a mutant EZH2 protein resistant to SAM-competitive inhibitors. Together, EED226 inhibits PRC2 activity via an allosteric mechanism and offers an opportunity for treatment of PRC2-dependent cancers. Currently, the two classes of PRC2 inhibitors are in clinical trial studies. We are further investigating the mechanism how the expression of PRC2 target genes was modulated by PRC2 inhibitors, to expand the potential indications and identify biomarkers for PRC2 inhibitors.

Concurrent Session 5: Plant Biology

Xuemei Chen – University of California-Riverside
Biogenesis and activities of plant microRNAs - The "Where" and "How"
MicroRNAs (miRNAs) impact nearly all biological processes by serving as sequence-specific regulators of gene expression. The biogenesis of miRNAs is a multi-step process involving the transcription of MIR genes into primary miRNAs (pri-miRNAs), the processing of pri-miRNAs into pre-miRNAs and then to miRNA/miRNA* duplexes, and the loading of miRNAs into an effector argonaute (AGO) protein. The miRNA-AGO complex regulates gene expression through degradation or translation repression of target mRNAs. Although major players mediating miRNA biogenesis or miRNA activities have been uncovered, where miRNAs are synthesized or act in the cell and how the subcellular sites affect miRNA activities are poorly understood. I will discuss our recent findings that implicate the nuclear pore and endoplasmic reticulum in the biogenesis/activities of plant miRNAs.

Xiaofeng Cao – Institute of Genetics & Developmental Biology, CAS
Mechanisms and functions of histone demethylases in Arabidopsis
Transcription activity of chromatin is regulated by covalent modifications on nucleosomes and DNA. Recent efforts have identified a lot of chromatin modifiers, which play important roles in various aspects of biological processes. These chromatin modifiers normally bind a subset of specific genomic loci. Discovering the mechanisms of recruiting these modifiers is essential for understanding the biological function of them. We previously identified Arabidopsis JMJ14, IBMI and REF6 as H3K4, H3K9 and K3K27 specific histone demethylases. In my presentation, I will discuss the molecular mechanisms of these proteins in substrate specificity and genome-wide targeting. I will also report JMJ16 as a new histone H3K4demethylase and discuss of its function in Arabidopsis.

Weicai Yang – Institute of Genetics & Developmental Biology, CAS
Pollen tube guidance in flowering plants: The interplay between male and female gametophytes
During evolution, novel reproductive structures and mechanisms have evolved to adapt to terrestrial land environment in plants. In angiosperms, such evolutionary development is manifested by the flower, multicellular gametophyte, double fertilization, loss of sperm motility, and siphonogamy in which the immotile sperm was delivered to the egg by a pollen tube produced by the male gametophyte (pollen), a process named pollen tube guidance (PTG). Previous studies suggested that PTG requires the intimate interactions between the pollen tube and maternal tissue of the pistil and the female gametophyte respectively. Although signaling molecules, such as LURE1 produced by the synergid of the female gametophyte to attract and guide the pollen tube growth, were identified, how the pollen tube recognizes and responds to the guiding molecule is not yet clear. Through genetic screen, we isolated a number of Arabidopsis mutants that disrupt PTG processes. *CCG*, a central cell-specifically expressed gene, is required for the female gametophyte to attract the pollen tube. *CCG* encodes a nuclear protein that regulates the expression of a number genes important for PTG via CBP1 which interacts with RNA polymerase II, the Mediator complex and AGL transcription factors in the central cells and also *LURE1* expression in the synergid indirectly. *POD1*, a pollen tube-expressed gene, is required for the male gametophyte to respond to the female signals. *POD1* encodes a ER protein that interact specifically with CRT3 which is implicated to control the folding of Leucine-Rich Repeat Receptor-Like Kinases. Recently, we also identified the male MDIS/MDIK receptor complex that recognizes the female attracting signals. At the same time, another LRR-RLK PRK6 has also been reported to be LURE1 receptor in Arabidopsis. These findings provide novel insight into mechanisms controlling PTG and will be discussed.

Yinong Yang – Pennsylvania State University
Efficient gRNA expression and multiplex genome editing based on endogenous tRNA

processing
The bacterial cluster regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein nuclease (Cas) system is a powerful and versatile molecular tool for genome engineering. To improve CRISPR/Cas-enabled multiplex genome editing, a polycistronic tRNA-gRNA (PTG) strategy was developed for efficient expression of multiple gRNAs based on the endogenous tRNA processing system. The PTG strategy has been effectively used for simultaneous editing of multiple genomic sites, deletion of chromosomal fragments, cis-element and promoter editing, temporal and spatial genome editing, multiplex base editing and other sophisticated CRISPR/Cas applications in various plant, animal or microbial systems. The PTG-mediated multiplex editing enables functional discovery of coding and non-coding DNA sequences in plants and will facilitates simultaneous editing and genetic improvement of multiple agronomic traits such as disease resistance, abiotic stress tolerance, nutrient use efficiency, yield and nutritional quality. With improved CRISPR/Cas tools and methods, multiplex editing is expected to open up a broad range of promising applications for genome engineering, functional genomics and precision breeding of agricultural crops.

Binglian Zheng – Fudan University
Paternal miR159 triggers endosperm nuclear division by clearing maternal block in Arabidopsis
Sperm entry triggers central cell division during seed development, but what factors besides the genome are inherited from sperm, and the mechanism by which paternal factors regulate early division events, are not understood. In my today's talk, I will discuss our recent finding that sperm miR159 promotes endosperm nuclear division through repressing maternal targets. Disruption of paternal miR159 caused seeds abortion, which resulted in arrested and/or delayed endosperm nuclear divisions. Mechanistically, loss of paternal miR159 led to retention of maternal MYB33 and MYB65, two miR159 targets, in the central cell after fertilization. Furthermore, ectopic expression of miR159-resistant version of *MYB33* (mMYB33) in the endosperm significantly inhibited the initiation of endosperm nuclear division. Thus, these results show that paternal miR159 inhibits its maternal targets to promote endosperm nuclear division, thus uncovering a previously unknown paternal effect on seed development.

Hongwei Guo –Southern University of Science and Technology
How Plant Smells: Signaling Mechanisms of Ethylene Gas
Ethylene is a unique phytohormone, which is a simple gas molecule that regulates a wide array of plant processes, including fruit ripening and abscission, leaf and flower senescence, stress tolerance and pathogen defense. We have demonstrated that plant responses to ethylene are mediated by the regulation of EBF1/EBF2-dependent proteasomal degradation of EIN3 and EIL1 transcription factors. EIN2, whose null mutant is completely insensitive to ethylene, acts as an essential ethylene signaling component. Recently, we found that, in the present of ethylene, the C-terminus of EIN2 (CEND) undergoes proteolytic cleavage, and subsequently translocates into the nucleus to promote the accumulation of EIN3/EIL1, as well as to induce the turnover of EBF1/EBF2 proteins. However, EIN2 CEND was found to package into discrete and prominent cytoplasmic foci apart from nuclear localization in response to ethylene. This raises the possibility that there must exist additional mode of EIN2 action other than its nuclear function in ethylene signaling cascade. We report a novel mechanism of EIN2-mediated ethylene signaling, whereby EIN2 imposes the translational repression of EBF1 and EBF2 mRNA. We find that the EBF1/2 3' untranslated regions (3'UTRs) mediate EIN2-directed translational repression, and identify multiple PolyU motifs as functional cis-elements of 3'UTRs. Furthermore, we demonstrate that ethylene induces EIN2 to associate with 3'UTRs and target EBF1/2 mRNA to cytoplasmic processing-body (P-body) through interacting with multiple P-body factors, including EIN5 and PABs. Our study illustrates the translational regulation as a key step in ethylene signaling, and represents the first demonstration of mRNA 3'UTR functioning as a "signal transducer" to sense and relay

cellular signaling in plants. New advances on ethylene signaling will also be discussed.

Dao-Xiu Zhou – Université Paris-sud 11, France

Dynamics of rice epigenomes in plant development and adaptation to environment

Chromatin-based epigenomes are essential for gene expression reprograming during development and adaptation to the changing environments in plants. Chromatin modifications such as DNA methylation and histone modifications consume important metabolites such as S-adenosyl methionine, acetyl coenzyme A, NAD+, alpha-ketoglutarate, etc. In the past years, we have characterized several rice epigenomes and studied reprograming mechanism of histone modifications involved in gene expression programs of plant development and response to stress. A set of chromatin modification and recognition enzymes (histone methyltransferases, demethylase, histone acetyltransferases and deacetylases, chromatin remodeling factors, etc.) have been studied. Recently we have been focusing our study on interplay between chromatin modification and energy metabolism in plant adaptation to environment. I will present our recent results on rice histone deacetylase function in regulation of plant metabolism and on genome-wide histone lysine acetylation and acylations (e.g. butyrylation and crotonylation) in responding to environmental/metabolic conditions.

Xuehua Zhong – University of Wisconsin-Madison, xuehua.zhong@wisc.edu

Epigenetic switch regulating floral phase transition

Epigenetic modification plays critical roles in many biological processes including genome integrity, development, environmental responses, and diseases. The overall goal of our research is to uncover how versatile developmental and environmental signals trigger epigenetic modifications, how cells are instructed to deposit the modification correctly in the genome, and how epigenetic mechanism enables the genome to generate adaptive responses. We address these questions at the whole genome level by combining functional genomics, genetic, proteomic, biochemical, cell biological, and structural approaches. Our lab recently discovered an epigenetic complex as a novel player in ribosome biogenesis as well as an epigenetic switch triggering developmental phase transition. I will discuss the data describing our latest understanding of the underlying mechanism.

Concurrent Session 6: Chromatin Remodeling and 3D Genome

Guohong Li – Institute of Biophysics, Chinese Academy of Sciences, China,
Structure and dynamics of 30-nm chromatin fibers in gene regulation

Zhiguo Zhang, Columbia University
DNA replication coupled nucleosome assembly in epigenetic inheritance and plasticity
Posttranslational modifications on histones including those in response to environmental stimuli and during development have a profound impact on gene expression states. Recently, it has been shown that at least some of these modifications are heritable during mitotic cell division and even through meiosis. As the "first" and rate-limiting step of transmission of these histone modifications, it is proposed that parental histone $(H3\text{-}H4)_2$ tetramers bearing modifications are randomly and equally distributed to leading and lagging strands of DNA replication forks, and serve as the "template" for copying these modifications onto nucleosomes containing newly synthesized $(H3\text{-}H4)_2$ tetramers. Because of duplication of DNA, newly synthesized histones $(H3\text{-}H4)_2$, which have distinct modifications from parental histones, are needed to fill in the gap. This dogmatic view is based largely on the isotope labeling experiments performed over 30 years ago showing that both daughter cells receive equal amount of parental $(H3\text{-}H4)_2$ tetramers. However, this model has not been tested *in vivo* in any eukaryotic cells due to challenges in monitoring histone segregation onto leading and lagging strands. Moreover, while several histone chaperones and histone modifying enzymes play important roles in regulating nucleosome assembly of newly synthesized $(H3\text{-}H4)_2$ tetramers, the molecular mechanisms underlying the transfer of parental histone $(H3\text{-}H4)_2$ tetramers onto replicated DNA remain largely unknown. In this meeting, I will summarize our recent studies on the analysis of the distribution of parental and newly synthesized $(H3\text{-}H4)_2$ onto leading and lagging strands (Yu e al Science 2018 and Gan et al Molecular Cell 2018) using the eSPAN (enrichment and sequencing of protein-associated nascent DNA) method (Yu et al Molecular Cell 2014), which can detect whether a protein is enriched at leading or lagging strands at a genome-wide scale. I will present experimental evidence indicating that parental $(H3\text{-}H4)_2$ tetramers are asymmetrically distributed onto leading and lagging strands, and that multiple mechanisms regulate nucleosome assembly of parental H3-H4 tetramers. I will speculate the implication of these findings in epigenetic inheritance during symmetric cell divisions and in epigenetic plasticity during asymmetric cell division.

Yijun Ruan – Jax Laboratory
Multiplexity in 3D genome organization and transcription regulation

Qing Li – Peking University, China
Decode the communication between histone chaperones and replisome components
In eukaryotic cells, DNA replication occurs in the context of chromatin environment. Our research aims to dissect the mechanisms of chromatin replication, to determine its role during epigenetic inheritance, and to explore the connections among epigenetic inheritance, genome stability maintenance and cell fate choice. Using budding yeast as a model, we have focused on determining how nucleosomes, the basic repeating units of chromatin, are assembled in a process that is coupled to DNA replication. This process is termed as DNA replication-coupled (RC) nucleosome assembly, and involves concerted interplay among diverse histone chaperones and replisome components. In this talk, I will discuss our recent progress on how histone chaperone FACT connects to DNA Pol□ during RC nucleosome assembly and how this "communication" contribute to chromatin replication.

Geno Yujiang Shi – Harvard University
Understanding the Epigenetic Basis Linking Pernicious Environment and Aging to Human Diseases

Yali Dou – University of Michigan
MLL1 in development and diseases

Wei Xie, Tsinghua University, China
Chromatin reprogramming during early animal development

Concurrent Session 7: Late-Breaking Session

George Fu Gao – Inst. of Microbiology, CAS
Medical Science Research and NSFC

Dihua Yu –MD Anderson Cancer Center
Tumor Microenvironment-derived Exosomes (EVs) in Metastasis and Immune Activation
Tumor cell-derived exosomes are well-known to promote tumor growth, angiogenesis, immune escape, drug resistance, and metastasis. However, the functions of tumor microenvironment (TME)-derived exosomes in tumor development were understudied. We have revealed critical contributions of TME-derived exosomes in brain metastasis and immune responses.
Brain metastases affect millions of cancer patients and have a < 20% one year survival rate. My team strived to gain global mechanistic understanding of brain metastasis to guide development of novel therapies for brain metastasis. Among many brain metastasis-specific gene alterations, we found that a severe PTEN-loss in brain-metastasis. Interestingly, the brain astrocyte-derived exosomes deliver miR-19a into brain metastatic cancer cells and reversibly downregulates PTEN expression in brain metastatic tumor cells. PTEN-loss in tumor cells led to increased CCL2 secretion and recruitment of myeloid cells to promote brain metastasis. Stable ablation of CCL2 inhibits brain metastasis in vivo, demonstrating the potential of targeting CCL2 for therapeutic intervention of life-threatening brain metastases.
Immunogenic tumor antigen presentation is a key determining step of effective cancer immunotherapy. Dendritic cells (DCs) are critical for cross-presentation of tumor antigens to activate T cells. Unfortunately, in most tumors, the available DCs are profoundly dysfunctional. Recently, we have developed novel approaches to enhance DCs antigen presentation function by increasing secretion of DC-derived exosomes, which subsequently led to more effective T cell-mediated tumor killing.
Our findings suggest that TME-derived exosomes may provide new paradigms for metastasis therapies, immune activation, and other anti-cancer strategies.

Chuan He –University of Chicago
RNA methylation in translation regulation

Weijun Pan -Shanghai Institutes of Biological Sciences, CAS
Vcam-1+ Macrophages Guide Homing of Haematopoietic Stem and Progenitor Cells into a Vascular Niche

Dong Li –Institute of Biophysics, CAS
Visualizing intracellular organelle and cytoskeletal interactions with grazing incidence structured illumination microscopy

Qing Zhang, University of North Carolina at Chapel Hill
Studying Oxygen Sensing Pathway in Cancer
Hypoxia is a characteristic of most solid cancers, which is associated with resistance towards radiation and chemotherapy. As tumors grow, they can sense the oxygen tension and reprogram critical pathways that are important for cancer cell survival and therapy resistance. One of examples is through upregulation of hypoxia inducible factor α (HIFα) and activation of HIF signaling downstream pathways. My lab is mainly interested in studying the oxygen-sensing pathway and how they contribute to the development of tumors as well as therapeutic resistance. One of the central players in this pathway is prolyl hydroxylase (EglN1, 2 and 3), a family of iron- and 2-oxoglutarate-depedent dioxygenases. EglNs can hydroxylate HIFα on critical proline residues, which will trigger von Hippel-Lindau (*VHL*)-associated E3 ligase complex binding and lead to HIFα degradation. One of research directions in the lab is trying to identify novel EglN prolyl hydroxylase substrates and

examine their role in cancer. The other direction is to focus on examining the VHL and its bona-fide substrates in kidney cancer. Overall, my lab currently studies hypoxia, prolyl hydroxylase and *VHL* signaling in cancer, especially breast and renal cell carcinomas. I will discuss our latest findings on these research area (including the latest paper in ***Science*** July 20, 2018) as well as other unpublished data from my lab.

Concurrent Session 8: Tumor immunology

Di Yu, Department of Immunology and Infectious Disease, John Curtin School of Medical Research, Australian National University

Follicular cytotoxic T cells: localisation, transcriptional regulation and implication for cancer immunotherapy

The importance of having specialised cytotoxic $CD8^+$ T cells in B cell follicles has only began to be appreciated. Recently, my group discovered a novel subset of cytotoxic $CD8^+$ T cells, termed 'follicular cytotoxic T cells' (TFC cells). We demonstrated that T_{FC} cells expressed B-cell follicle-homing chemokine receptor, CXCR5, which enables them to migrate to B cell follicles and eliminate infected follicular helper T (T_{FH}) cells and B cells. Intriguingly, T_{FC} cells showed a distinct memory-like phenotype, characterised by the high expression of memory-associated transcription regulators Tcf1, Bcl6 and Id3 but the low expression of Blimp1 and Id2, required for the effector differentiation of $CD8^+$ T cells. Together with several studies from other groups, T_{FC} cells were shown to possess the capability for self-renewal and undergo a proliferative burst after anti-PD-1/PD-L1 therapy. In this talk, I will discuss the current understanding of T_{FC} cells and the potential of potentiating T_{FC} cells for cancer immunotherapy.

Penghui Zhou, Sun Yat-sen University Cancer Center, Guangzhou, China

Identification of Cancer Immunotherapy Targets

Recent successes of immunotherapies in clinic generated tremendous enthusiasm in the cancer immunotherapy field. However, the tumor microenvironment severely impeded immune responses against cancer via multiple mechanisms. In particularly, the regulatory switches controlling T-cell function in immunosuppressive tumours are not well understood. Here we show that such inhibitory mechanisms can be systematically discovered in the tumour microenvironment. We devised an in vivo pooled short hairpin RNA (shRNA) screen in which shRNAs targeting negative regulators became highly enriched in murine tumours by releasing a block on T-cell proliferation upon tumour antigen recognition. Such shRNAs were identified by deep sequencing of the shRNA cassette from T cells infiltrating tumour or control tissues. One of the target genes was Ppp2r2d, a regulatory subunit of the PP2A phosphatase family. In tumours, Ppp2r2d knockdown inhibited T-cell apoptosis and enhanced T-cell proliferation as well as cytokine production. Key regulators of immune function can therefore be discovered in relevant tissue microenvironments.

Chengcheng "Alec" Zhang, UT Southwestern

Targeting ITIM-receptors for leukemia treatment

Inhibitory leukocyte immunoglobulin-like receptors (LILRBs 1-5) transduce signals via intracellular immunoreceptor tyrosine-based inhibitory motifs (ITIMs) that recruit protein tyrosine phosphatase non-receptor type 6 (PTPN6 or SHP-1), protein tyrosine phosphatase non-receptor type 11 (PTPN11 or SHP-2), or Src homology 2 domain-containing inositol phosphatase (SHIP), leading to negative regulation of immune cell activation. Certain of these receptors also play regulatory roles in neuronal activity and osteoclast development. The activation of LILRBs on immune cells by their ligands may contribute to immune evasion by tumors. Recent studies found that several members of LILRB family are expressed by tumor cells, notably hematopoietic cancer cells, and may directly regulate cancer development and relapse as well as the activity of cancer stem cells. LILRBs thus have dual concordant roles in tumor biology – as immune checkpoint molecules and as tumor-sustaining factors. Importantly, the study of knockout mice indicated that LILRBs do not affect hematopoiesis and normal development. Therefore LILRBs may represent ideal targets for tumor treatment that combines targeted therapy and immunotherapy. I will discuss recent progress about the roles of LILRBs and ITIM-receptors in leukemia development.

Pan Zheng, University of Maryland Baltimore

Targeting host defense on DAMPs to prevent immunotherapy related adverse events

Anti-CTLA-4 monoclonal antibodies (mAbs) confer a cancer immunotherapeutic effect (CITE) but cause severe immunotherapyrelated adverse events (irAE). Targeting CTLA-4 has shown remarkable long-term benefit and thus remains a valuable tool for cancer immunotherapy if the irAE can be brought under control. An animal model, which recapitulates clinical irAE and CITE, would be valuable for developing safer CTLA-4-targeting reagents. We developed a model using mice harboring the humanized Ctla4 gene to study irAE. In this model, the clinically used drug, Ipilimumab, induced severe irAE especially when combined with an anti-PD-1 antibody. The irAE corresponded to systemic T cell activation and resulted in reduced ratios of regulatory to effector T cells (Treg/Teff) among autoreactive T cells. Using mice that were either homozygous or heterozygous for the human allele, we found that the irAE required bi-allelic engagement, while CITE only required monoallelic engagement. Our data demonstrate that complete CTLA-4 occupation, systemic T cell activation and preferential expansion of self-reactive T cells are dispensable for tumor rejection but correlate with irAE. Damage related molecular patterns (DAMPs) play an important role in regulating tissue damages, antigen presenting cells activation and effector T cell functions. Our previous work demonstrated that CD24- Siglec signaling pathway suppresses inflammation triggered by DAMPs. We will present the data on the role of DAMPs-binding protein CD24 and Siglecs in irAE pathogenesis.

Concurrent Session 9: Molecular and Cellular Mechanisms of Neurodegeneration

Boxun Lu – School of Life Sciences, Fudan University, Shanghai

Allele-selective Degradation of Mutant HTT (mHTT) via Autophagy by mHTT-LC3 Linker Compounds

Reducing the disease-causing protein levels by low-molecular-weight compounds is an attractive approach to treat relevant diseases. To achieve this goal, we hypothesized that linker compounds interacting with both the disease protein and the key autophagosome protein LC3 may target the disease protein for clearance by autophagy to reduce their levels. We tested this concept using the mutant HTT protein (mHTT), which causes Huntington's disease (HD), an incurable neurodegenerative disorder. By compound-chip based high-throughput screening, validation and structural optimization, we identified two linker compounds that interact with both LC3 and mHTT, but not wild-type HTT (wtHTT). Both compounds targeted mHTT for autophagy-mediated degradation and reduced mHTT levels in HD cells and animals, while they had minimal effect on the wtHTT level, achieving allele-selective lowering of mHTT. Importantly, these compounds rescued HD-relevant phenotypes in HD cells and animals, confirming therapeutic potential of these compounds. Our study demonstrates the concept of treating incurable diseases by compounds that crosslink LC3 and the disease-causing proteins, with the potential of achieving allele-selective lowering of the target protein.

Zhenyu Yue - Departments of Neurology and Neuroscience, Icahn School of Medicine at Mount Sinai, New York

Regulation of a Synuclein Transmission by Glial Autophagy in CNS

The formation of Lewy bodies, primarily composed of oligomerized α-synuclein, is a pathological hallmark of Parkinson's disease (PD) and dementia with Lewy bodies (DLB). The emerging evidence from multiple lines of research has provided a support to the Braak's hypothesis of spreading of Lewy body pathologies in human involving inter-cellular transmission of □-synuclein aggregates. The advances in genetics and experimental model systems have revealed an important role for defects in intracellular transport pathways including autophagy-lysosomes in PD pathogenesis. Autophagy is a cellular degradation pathway for the clearance of protein aggregates and injured organelles. The importance of autophagy in degradation of disease form α-synuclein and therefore neuroprotection has been extensively studied in neurons; however, the role for glial autophagy remains elusive. Herein we have characterized the role for microglial autophagy in internalizing and degrading different forms of α-synuclein in cultures and genetic animal models. Our studies show that microglia actively take up specific form α-synuclein through pattern recognition receptors, which trigger selective autophagy signaling to digest phagocytosed α-synuclein. Our data therefore demonstrates roles for microglial autophagy in not only controlling homeostasis and spreading of α-synuclein but also regulating immune response of microglia exposed to disease proteins.

Xiangdong William Yang - Department of Psychiatry & Biobehavioral Sciences, David Geffen School of Medicine, UCLA, Los Angeles.

Microglial Reprogramming to Ameliorate Pathological Phenotypes in Alzheimer's Disease

Human genetic studies of late-onset Alzheimer's disease (AD) reveal more than a dozen risk or protective genes with enriched expression in the brain's innate immune cells, microglia. Among these genes, variants of Triggering Receptor Expressed on Myeloid Cells 2 (TREM2) confer the second highest risk for the late-onset AD. Loss-of-function of TREM2 impairs the ability of microglia to encircle and engulf the amyloid plaques, and proper upregulation of the transcriptional program in the disease-associated microglia. However, it remains unclear if TREM2 function could be modulated to mitigate amyloid pathology and neuronal injury in AD model organisms. Here we show that elevated TREM2 gene dosage, through BAC-mediated transgenesis in mice (BAC-TREM2), could modify the disease pathogenesis in two amyloid

transgenic mouse models. Elevated TREM2 expression can ameliorate multiple AD-related phenotypes in the disease models, including amyloid plaque load, dystrophic neurites, and cognitive impairment. Interestingly, both transcriptomic and microglial morphological studies suggest elevated TREM2 gene-dosage results in the reprogramming of the reactivity of the plaque-associated microglia. Finally, our latest evidence suggests an AD-associated TREM2 risk variant is hypofunctional and cannot elicit the microglial reprogramming effects *in vivo*. Together, our study uncovers a novel role of TREM2 in reprogramming the microglial responsivity and reducing amyloid-associated toxicities in Alzheimer's disease.

Junmin Peng - Departments of Structural Biology and Developmental Neurobiology, Center for Proteomics and Metabolomics, St. Jude Children's Research Hospital, Memphis, TN;
High Throughput Proteomics Approach to Understanding Alzheimer's Disease
My research goal is to develop mass spectrometry-based proteomics and systems biology approaches to address biomedical challenges. We have developed a quantitative proteomics pipeline, capable of analyzing >10,000 proteins and dissecting tens of thousands of posttranslational modifications from relevant cellular and animal models as well as human clinical specimens. Integration of such large-scale omics data offers a holistic view for unbiased identification of central disease gene/protein networks. To understand the pathogenesis of Alzheimer disease (AD), the most common form of dementia, we profiled aggregated proteome in all common neurodegenerative diseases, including AD, mild cognitive impairment, Parkinson disease, Lewy body dementia, Ub-positive frontotemporal lobar degeneration, amyotrophic lateral sclerosis, and corticobasal degeneration. This comprehensive study identified the accumulation of U1-70K and other U1 snRNP spliceosome components in AD. Multiple U1 snRNP subunits form cytoplasmic tangle-like structures in AD but not in other diseases. RNAseq analysis reveals dysregulated RNA processing with accumulation of unspliced RNA species in AD. Thus, our results demonstrate unique U1 snRNP pathology and suggest abnormal RNA splicing in AD. Furthermore, we have generated a brain-specific transgenic mouse model for deregulating the U1-70K activity. The transgenic mice recapitulate many AD features, supporting the role of RNA dysregulation in Alzheimer's disease.

Zhentao Zhang – Renmin Hospital of Wuhan University
δ-secretase-cleaved Tau Stimulates Aβ Production via Upregulating STAT1-BACE1 signaling in Alzheimer's Disease
δ-secretase, an age-dependent asparagine protease, cleaves both amyloid precursor protein (APP) and Tau and is required for amyloid plaque and neurofibrillary tangle pathologies in Alzheimer's disease (AD). However, whether δ-secretase activation is sufficient to trigger AD pathogenesis remains unknown. Here we show that the fragments of δ-secretase-cleavage, APP (586-695) and Tau(1-368), additively drive AD pathogenesis and cognitive dysfunctions. Tau(1-368) strongly augments BACE1 expression and Aβ generation in the presence of APP. The Tau(1-368) fragment is more robust than full-length Tau in binding active STAT1, a BACE1 transcription factor, and promotes its nuclear translocation, upregulating BACE1 and Aβ production. Notably, Aβ-activated SGK1 or JAK2 kinase phosphorylates STAT1 and induces its association with Tau(1-368). Inhibition of these kinases diminishes stimulatory effect of Tau(1-368). Knockout of STAT1 abolishes AD pathologies induced by δ-secretase-generated APP and Tau fragments. Thus, we show that Tau may not only be a downstream effector of Aβ in the amyloid hypothesis, but also act as a driving force for Aβ, when cleaved by δ-secretase.

Xiao-Jiang Li - Department of Human Genetics, Emory University, Atlanta; GHM Institute of CNS Regeneration, Jinan University, Guangzhou
Genetically Modified Large Animal Models of Brain Diseases
Genetically modified animal models have been extensively used to investigate the pathogenesis of age-dependent neurodegenerative diseases, such as Alzheimer (AD), Parkinson (PD), Huntington (HD) diseases, and Amyotrophic lateral sclerosis (ALS). The

common feature of these diseases is the age-dependent accumulation of misfolded proteins in the brain, which can be recapitulated in a variety of mouse models of neurodegenerative diseases. However, the brains of transgenic mouse models of AD, PD, and HD do not show the striking neuronal loss or degeneration that is a typical pathological feature in patient brains. Species differences between small animals and humans may account for differential pathology in transgenic mouse models and patient brains. Using CRISPR/Cas9 to modify the endogenous disease genes in large animals (pigs and monkeys), we demonstrate that typical neuropathological features can be mimicked in the brains of large animals. The findings underscore the importance of using large mammals to investigate the pathogenesis of important brain diseases and

Concurrent Session 10: Chemical Biology

Peng Chen, Peking University
Bioorthogonal Cleavage Reactions in Space and Time: from Living Cells to Living Animals
Employing small molecules or chemical reagents to modulate the function of an intracellular protein of interest, particularly in a gain-of-function fashion, remains highly desired but challenging. In this talk, I will introduce a "genetically encoded chemical decaging" strategy that relies on our developed bioorthogonal cleavage reactions to control protein activation in living systems with high spatial and/or temporal resolution. These reactions exhibited high efficiency and low toxicity for chemical decaging of the masked-lysine residue on intracellular proteins, which is complementary to the previously used photo-decaging reactions. We are currently employing this method to block specific kinase's activity in living cells, which allowed the subsequent gain-of-function study of individual kinase within the intracellular signaling transduction network. Our efforts on exploring the therapeutic potential of these novel reactions for pro-drug activation will also be discussed.

Huiwang Ai – University of Virginia
A general strategy to red-shift green fluorescent protein based biosensors
In the past two decades or so, a large number of green fluorescent biosensors have been developed and catalyzed biological research in various areas. Compared to green fluorescent ones, red fluorescent biosensors are preferable because of lower phototoxicity and increased tissue penetration of longer wavelength photons. Although recent studies have developed a few fluorescent biosensors based on red fluorescent proteins, each required extensive optimization effort. I will present a general and convenient method to convert green fluorescent proteins and green fluorescent protein based biosensors into red ones.

Hang Hubert Yin – Tsinghua University
Small Molecule Immunomodulators that Target Toll-Like Receptors
The protein-protein and protein−nucleic acid interfaces have been regarded as "undruggable" despite their importance in many biological processes. The toll-like receptors (TLRs) provide exciting targets for a number of autoimmune diseases, infectious diseases, pain management, and cancers. Using multidisciplinary approaches, we have successfully developed novel exogenous small molecule probes that were shown to be competitive inhibitors or activators of various TLRs with high affinity and specificity. Some of the lead compounds are currently in the pipeline for further drug discovery.

Xi Chen – University of California-Davis
Chemoenzymatically synthesized carbohydrates as chemical biological probes and potential prebiotics
Carbohydrates are the most abundant organic compounds on earth. They play important roles in biology and pathology. We have developed highly efficient one-pot multienzyme (OPME) systems for synthesizing structurally complex naturally occurring carbohydrates and their non-natural derivatives. These compounds have been used as chemical biological probes and potential prebiotics. Our recent collaboration work on the applications of chemoenzymatically synthesized carbohydrates will be presented.

Yinsheng Wang – University of California Riverside
Quantitative proteomics for interrogating novel nucleic acid-binding proteins
The functions of nucleic acids involve their interactions with cellular proteins. In this presentation, I will discuss about our recent efforts toward the development and applications of quantitative proteomic methods for unbiased, proteome-wide discovery of proteins that can recognize unique secondary structures of DNA. I hope to illustrate that the method constitutes a power tool for discovering novel nucleic acid-binding proteins and for revealing

their functions in cells.

Caiguang Yang – Shanghai Institute of Materia Medica

Tackling untargeted protein in RNA epigenetics

RNA epigenetics is a fast-moving field in biology and represents a new layer of regulation of genetic information. METTL3 and METTL14, the m6A methyltransferases, has been reported to control and/or maintain myeloid leukemia, highlighting their oncogenic roles in leukemogenesis. In addition, the first identified m6A demethylase FTO has also been found to play an oncogenic role in a subset of AML and by suppression of FTO activity, 2HG exhibits obvious anti-tumor effects in AML and brain tumors. However, at this moment few inhibitors have been characterized and less is known about the potential clinical applications of inhibiting RNA epigenetics compared to DNA or histone epigenetics. To this end, high-quality inhibitors for FTO demethylation represent unmet needs for m6A modulation in RNA epigenetics and for target identification in cancer drug discovery.

We identified the first FTO inhibitor through virtual screening, while rhein shows modest selectivity for AlkB demethylases. Then, we took the advantage of the structural differences between the two RNA demethylases FTO and ALKBH5, used for substrate recognition, and repositioned meclofenamic acid (MA), an anti-inflammatory drug, to a selective inhibitor for FTO demethylation. However, the cellular activity of MA needs to be largely improved, and the target engagement remains poorly understood.

Here we report the development of two promising, selective, and potent FTO inhibitors (namely FB23 and FB23-2), through structure-guided design, that apparently binds to the FTO protein and selectively inhibits its catalytic demethylation activity. FB23-2 efficiently suppresses the proliferation viability of AML cells, and significantly delays leukemogenesis in vivo. Interestingly, the efficacy of FB23-2 was also tested in additional in vitro and in vivo patient-derived AML models. This study implies that FTO demethylation would be viewed as a druggable target and small-molecule inhibitors of FTO that modulate epitranscriptome would be potential candidates for a targeted therapy of AML. As FTO demethylation has also been linked to various types of cancers, our findings may have a broad impact on cancer therapy by targeting the epitranscriptome.

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Concurrent Session 11: Cell Microenvironment and Diseases

Chuanyue Wu, Southern University of Science and Technology
"Cell-extracelluar matrix adhesion: molecular basis, signaling and diseases"
My laboratory is interested in the molecular mechanisms that govern integrin-mediated cell-extracellular matrix adhesion and signaling as well as human diseases that are associated with alterations of cell-extracellular matrix adhesion. Integrin-mediated cell-extracellular matrix adhesion is a fundamental process that controls a variety of processes including cell proliferation, differentiation, migration and survival. Alterations of cell-extracellular matrix adhesion and signaling are intimately associated with the pathogenesis and progression of common human diseases including cancer, kidney and skeletal diseases. Thus, elucidating the molecular basis underlying integrin-mediated cell-extracellular matrix adhesion and signaling, and developing therapeutic approaches that target key cell-extracellular matrix signaling proteins are important areas of current biomedical research. In this talk, I will discuss some of our recent work on the functions of focal adhesion protein complexes in integrin-mediated signaling as well as their roles in the pathogenesis of human diseases.

Weiguo Zhu, Shenzhen University
"Histone modification and DNA damage repair"
Ataxia-telangiectasia mutated (ATM) is an apical kinase in the cellular response to DNA damage in eukaryotes, especially DNA double-strand breaks (DSBs). Upon DSB, ATM is activated through a hierarchy of well-organized cellular machineries, including post-translational modifications (PTMs), the MRE11-RAD50-NBS1 (MRN) complex, chromatin perturbations, and so on. Activation of ATM initiates a cascade of chromatin modifications, nucleosome remodeling and assembly of repair factors to ensure a highly orchestrated response and repair of the damaged DNA. Despite that numerous studies have tried to elucidate the mechanisms of ATM activation, how it is activated by DNA damage signals is still not fully understood. Among the various factors regulating ATM activation, histone modification has been considered essential, as histone octamer constitutes the core of nucleosome and histone tails protrude into the DNA strands to alter chromatin landscape and DNA accessibility. Here, I would like to present the proceedings of how histone modifications regulate ATM activation and inactivation, with an emphasis on the functional relevance in DNA damage response and repair.

Guozhi Xiao, Southern University of Technology
Osteocytic Kindlin-2 signaling modulates bone marrow microenvironment to regulate bone remodeling
Osteocytes embedded in a mineralized bone matrix regulate bone homeostasis in response to mechanical and biological signals by currently unknown mechanisms. This study shows that osteocytes express abundant Kindlin-2, a focal adhesion molecule, and that deleting Kindlin-2 in osteocytes in mice causes severe osteopenia throughout life and essentially abolishes the skeletal response to mechanical loading to increase bone mass and bone mineral density. Of particular clinical significance, Kindlin-2 loss in osteocytes largely impairs the anabolic actions of intermittent parathyroid hormone (PTH), the most potent anabolic bone agent currently available for osteoporosis treatment. Kindlin-2 loss in osteocytes not only drastically decreases osteoblast number and function, leading to reductions in osteoid production mineralization and bone formation, but also promotes osteoclast formation and bone resorption. Our in vitro and in vivo studies demonstrate that Kindlin-2 suppresses sclerostin expression in osteocytes and increases the level of □-catenin protein in osteoblasts and bone formation. Osteocytic Kindlin-2 signaling is critical for maintaining a proper bone microenvironment that promotes osteoblastic, but inhibits adipogenic, differentiation of mesenchymal stem cells. Kindlin-2 additionally inhibits Rankl expression in osteocytes and thereby osteoclast formation and differentiation from the bone marrow monocytes. Finally, Kindlin-2 signaling promotes osteocyte spreading and formation of the

dendrites and protects osteocytes from apoptosis. These studies uncover a previously unknown key function for Kindlin-2 and define distinct novel mechanisms through Kindlin-2 for osteocyte regulation of bone homeostasis.

Yi Sun, ZheJiang University

"The FBXW2-Catenin-MMPs axis regulates tumor invasion and metastasis"

Our recent study showed that FBXW2, an F-box E3 ubiquitin ligase, acts as a tumor suppressor to inhibit growth and survival of lung cancer cells by targeting SKP2 for degradation (1). Whether and how FBXW2 regulates tumor invasion and metastasis is previously unknown. Here, we report that FBXW2 is a novel E3 for targeting oncogenic protein β-catenin. FBXW2 binds to β-catenin upon EGF-AKT1-mediated phosphorylation on Ser^{552}, and promotes its ubiquitylation and degradation. Manipulation of FBXW2 expression negatively modulates β-catenin levels and its protein half-life. Functionally, ectopic FBXW2 expression inhibits migration and invasion by blocking transactivation of MMPs driven by β-catenin, whereas FXBW2 knockdown promotes migration, invasion and metastasis significantly both *in vitro* and *in vivo* lung cancer models. Finally, in human lung cancer specimens, endogenous FBXW2 levels are inversely correlated with β-catenin levels and lymph-node metastasis. Collectively, our study revealed a novel function and associated mechanism by which FBXW2 inhibits tumor migration, invasion and metastasis in lung cancer cells by targeting ubiquitylation and degradation of β-catenin.

Concurrent Session 12: Cancer Therapy

Chenghua Yang, Shanghai Institute of Nutrition and Health, CAS
Development of Bcl10 peptide inhibitors for the treatment of ABC-DLBCL
The CARMA1-Bcl10-MALT1 (CBM) complex functions as a central hub in NF-κB signaling pathway. Aberrant activity of this complex is involved in the pathogenesis of activated B cell-like diffuse large B-cell lymphomas (ABC-DLBCLs), the most aggressive and chemoresistant form of DLBCL. The activity of the CBM complex depends on the polymerization and filament formation of Bcl10. Here we developed a series of peptides that featured direct binding to Bcl10 and potent inhibition of its filament formation. Among these, Bcl10 inhibitory peptides Bcl10-P2 and Bcl10-P4 suppressed the enzymatic activity of MALT1 as well as the activity of NF-κB signaling pathway. By converting them to D-amino acid and retro configuration (DRI), we further enhanced their stability without impairing their activities. Importantly, DRI forms of Bcl10-P2 and Bcl10-P4 displayed highly specific inhibitory activity against the growth of ABC-DLBCL cells in vitro and in mouse xenograft models by suppression of cell proliferation and induction of apoptosis. Thus, our study developed a novo strategy to target Bcl10 by inhibitory peptides, which may provide a promising therapeutic strategy for ABC-DLBCL as well as other NF-κB dependent malignancies.

Zhijie Chang, Tsinghua University
"**Regulation of cell proliferation by a novel family protein p15RS and CREPT**"
We cloned a novel gene CREPT (*C*ell-cycle *R*elated and *E*xpression-elevated *P*rotein in *T*umor) based on a homology screen using p15RS. Our results revealed that p15RS negatively regulates Cyclin D1 expression, functioning as an intrinsic inhibitor for the canonical Wnt/□-catenin signal pathway. Interestingly, we observed that over-expression of CREPT enhanced cell proliferation by promoting cell cycle related genes including Cyclin D1. CREPT interacts with RNA polymerase II (RNAPII) and promotes the formation of a chromatin loop. We proposed that CREPT mediates a loop formation for the transcription termination as it prevents RNAPII from reading through the poly-A signal at the 3'-end termination site. CREPT is highly expressed in human tumors and the positive CREPT staining is significantly correlated with shorter survival time of the patients after surgery and treatment. We prospected that CREPT, functioning oppositely to p15RS, may be used as a marker for tumor diagnosis and a therapeutic target.

Zhang Jian, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China
"First-in-class Drug Design and Discovery"
Drug design method has been widely used to rationally create drug candidates, specially the combination of drug design, medicinal chemistry, and pharmacological evaluation helped more than 20 drugs reach the global market. However, more than 60% potential targets are still orphan due to their undruggable features. To make these targets druggable, we developed a series of drug design methods including recognition of protein-protein interaction, identification of allosteric site and allosteric drug screening to overcome the inaccessibility of the targets in the drug discovery. Inspired by the advantage of the methods, novel activators/inhibitors were discovered by our group in several drug targets and used to address the challenges of finely-tuned biological regulation and human disorder treatment and medicine, for example APC-Asef interaction inhibitor. The binding of APC to its receptor Asef relieves the negative intramolecular regulation of Asef and leads to aberrant migration in human colorectal cancer. Due to its crucial role in metastatic dissemination, the interaction between APC and Asef is an attractive target for anti-colorectal cancer therapy. Using an interface-induced method, we rationally designed a series of peptidomimetics that act as potent inhibitors of the APC interface. Crystal structures, biochemical, and cellular assays revealed that the peptidomimetics in the APC pocket inhibited colorectal cell migration by disrupting APC-Asef interaction. This work demonstrated the feasibility of using the APC-Asef interaction as a target to regulate colorectal cancer migration and provided the first class of protein-protein interaction inhibitors available for the development of APC-Asef signaling cancer therapeutics.

Quan Zhao, The State Key Laboratory of Pharmaceutical Biotechnology, School of Life Sciences, Nanjing University, Nanjing, China.

"Roles of NatD-mediated N-alpha-terminal acetylation of histone H4 in cancer metastasis"

Protein N-alpha-terminal acetylation (Nt-acetylation) is catalyzed by N-alpha-acetyltransferases (NATs). NatD, one of the most selective NATs, mediates Nt-acetylation of histone H4. NatD acts as a sensor of cell growth in yeast and is involved in apoptosis. However, the pathological role and the regulatory mechanism of NatD in cancers remain largely unknown. Here, we show that silencing NatD Suppressed the migratory and invasive capabilities of lung and breast cancer cells both in vitro and in vivo. However, different mechanisms were proposed controlling the progression of different cancers. These findings support that NatD is a key epigenetic regulator of cancer metastasis.

Hong-Jian Zhu, *Cancer Signalling Research Laboratory*
Department of Surgery (RMH), The University of Melbourne, Melbourne, Victoria 3050 Australia

"Exosomes and TGF-□ in Cancer: Biomarkers, Metastasis and Therapeutics"

Targeted therapy, or so-called magic bullet is one of the most outstanding successes in cancer treatments today. It results from the discovery of precise molecular causes of diseases. Transforming growth factor-□ (TGF-□) signaling pathway is one of the most important molecular drivers of cancer metastasis as we know and consequently 20+ clinical trials targeting its signaling for cancer treatment have been conducted. However the outcomes are poor. This points to the inaccuracy of our current understanding of molecular steps as the causes of cancer progression. Understanding the true molecular causes of TGF-□ signaling amplification is therefore critical to enable us to successfully target the pathway for cancer treatment. Here we describe TGF-□ in the form of exosomes and how exosome traffic, secretion and uptake amplify TGF-□ signaling in cancer cells. In addition, TGF-□ exosomes are the key mediator of the interaction between tumors and cancer-associated fibroblasts (CAFs), which facilitates cancer progression. Most importantly, was have found that TGF-□ signaling and its biological functions can be targeted by blocking exosome traffic, secretion and uptake. As such, exosomes are at the heart of cancer cell TGF-□ signaling amplification, defining the real cause of cancer progression, identifying mediators of cancer cell interaction with its microenvironment, and establishing new practical cancer treatment targets.

Hong-Jian Zhu, *Cancer Signalling Research Laboratory*
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TGF-□ signaling amplification, defining the real cause of cancer progression, identifying mediators of cancer cell interaction with its microenvironment, and establishing new practical cancer treatment targets.

Concurrent Session 13: Abstract Session

Jun Sun – UNIVERSITY OF ILLINOIS AT CHICAGO

Vitamin D receptor is required to protect from tumorigenesis and dysbiosis via the JAK/STAT pathway

Vitamin D exerts its regulatory roles in mucosal immunity, host defense, and inflammation via vitamin D receptor (VDR). Low VDR expression and diminished vitamin D/VDR signaling are observed in patients with colon cancer. Intestinal epithelial cells are constantly exposed to microbes and equipped with sophisticated protection mechanisms. Nevertheless, how intestinal epithelial VDR is involved in the maintenance of intestinal and microbial homeostasis remains largely unknown. Human VDR gene is a key host factor to shape gut microbiome (Wang, et al., Nature Genetics 2016). Further, we have shown that intestinal epithelial VDR conditional knockout (VDRΔIEC) leads to dysbiosis (imbalanced microbiome) (Wu, et al., Gut 2015). The JAK/STAT pathway plays a critical role in intestinal and microbial homeostasis. In the current study, we hypothesized intestinal VDR protects mice from dysbiosis via modulating the JAK/STAT pathway in tumorigenesis. We studied the mechanism whereby intestinal epithelial VDR suppresses tumorigenesis, using cell culture, colonoids, conditional intestinal epithelial knockout mice, and human samples. We reported that VDRΔIEC mice have higher tumor numbers with tumor location shifted from distal to proximal colon. Fecal microbiota analysis showed that lacking VDR leads to bacterial profile shift from normal to susceptible carcinogenesis. We found enhanced bacterial staining in mouse tumors. These data are consisted with our findings in human tumor sample. VDR deletion decreased Jak2 at protein and mRNA levels. By CHIP assay, we identified that VDR protein bound to the Jak2 promoter, suggesting that VDR transcriptionally regulated Jak2. Taken together, our observations suggest that absence of intestinal epithelial VDR leads to dysbiosis and susceptibility to colon cancer via reduced JAK/STAT signaling. Our study provides new insight into the molecular mechanism of VDR regulating the JAK/STAT pathway in microbiome-host interactions and tumorigenesis. Our studies also indicate a new target—microbiome and VDR signaling for prevention of cancer.

Jiahong Lu – Institute of Chinese Medical Sciences, University of Macau

Enhancing apoptotic cell clearance for inflammatory bowel disease intervention: a lesson from NRBF2 deficient mice

Autophagy dysfunction has been connected to inflammatory bowel disorder (IBD). NRBF2, a new component of Beclin-VPS34 complex, positively regulates autophagy through yeast to mammals. We find loss of NRBF2 sensitized mice to dextran sulfate sodium (DSS)-induced UC mouse model with dramatic accumulation of apoptotic cells in colon tissue. Functional study revealed a critic role for NRBF2 in regulating apoptotic cell clearance from *in vitro* to *in vivo* to eliminate the pro-inflammatory cytokine release. Mechanistically, NRBF2 is required for Mon1-Ccz1 guanine nucleotide exchange factor (GEF) activity to generate active Rab7 (GTP-bound form) for phagosome maturation. Samples from ulcerative colitis (UC) patients' colon tissue revealed the high co-efficiency of apoptotic cells accumulation and disease severity which is consistent with our observation in animal model. More importantly, NRBF2 expression level is up regulated in the colon tissue of UC patients and the NRBF2 positive cell number negatively co-related with the disease severity, indicating a protective role for NRBF2 in UC. Finally, to prove the concept that enhancing apoptotic cell clearance will prevent intestinal inflammation, we identified a small molecule compound from Chinese medicine plant Huanglian (a traditional Chinese medicine used for colitis treatment) which efficiently promoted macrophage-mediated apoptotic cell clearance and tested it on the experimental colitis model. The results showed that the compound significantly relieved the colitis lesion in animal model. Taken together, our study revealed a novel role for NRBF2 in regulating apoptotic cells clearance to maintain intestine homeostasis and suggest a new therapeutic strategy against IBD by enhancing apoptotic cells clearance.

Fei Li – Department of Biology, New York University
Heterochromatin regulate centromeres by protecting CENP-A from ubiquitin-mediated degradation
Centromere is a specialized chromosomal domain that is essential for faithful chromosome segregation during mitosis and meiosis. Most eukaryotes contain large and complex "regional" centromeres that are defined epigenetically by a conserved histone 3 variant, CENP-A. Regional centromeres are usually surrounded by the densely packed heterochromatin domain. Heterochromatin contains distinct epigenetic marks, such as histone H3K9 methylation. The exact role of heterochromatin in centromere assembly remains elusive. Unlike other eukaryotes, the budding yeast Saccharomyces cerevisiae has genetically-defined point centromeres. The transition between regional centromeres and point centromeres is considered as one of the most dramatic evolutionary events in centromere evolution. Here we demonstrated that Cse4, the budding yeast CENP-A homolog, can localize to centromeres in fission yeast and functionally substitute fission yeast CENP-A homolog, Cnp1. But overexpression of Cse4 results in its localization to heterochromatin. Cse4 is subject to efficient ubiquitin-dependent degradation in S. pombe, and its N-terminal domain of Cse4 dictates its centromere distribution via ubiquitination. Notably, without heterochromatin and RNA interference (RNAi), Cse4 fails to associate with centromeres. We showed that RNAi-dependent heterochromatin mediates centromeric localization of Cse4 by protecting Cse4 from ubiquitin-dependent degradation. Heterochromatin also contributes to the association of native Cnp1 with centromeres via the same mechanism. These findings suggest that protection of CENP-A from degradation by heterochromatin is a general mechanism used for centromere assembly, and also provide novel insights into centromere evolution.

Zhihua Wang – Wuhan University Renmin Hospital
Increased transcription and translation rates in cardiac hypertrophy are regulated by lncRNAs
Pathological cell growth during cardiac hypertrophy is characterized by faster transcription and translation rates; however, little is known about the molecular mechanism governing these processes. Using two screening strategies including RNA sequencing and genome-wide association study, we identified two crucial lncRNAs, termed Chaer (cardiac hypertrophy associated epigenetic regulator) and Miat (myocardial infarction associated transcript), that both contribute to the development of cardiac hypertrophy. Genetic knockout and siRNA-mediated silencing of Chaer significantly reversed the pathological gene expression reprogramming and the resultant heart dysfunction in trans-aortic constriction (TAC)-induced cardiac hypertrophy. RNA immunoprecipitation and tagged RNA pull-down assays identified EZH2, the catalytic subunit of PRC2, to be the direct target, which bound to a 66-mer motif of Chaer. This interaction was transiently enhanced upon hypertrophic stimulation, and interfered with PRC2 localization to the promoter region of pathological genes and subsequently released the epigenetic restriction of their expression. These data suggest an epigenetic checkpoint defined by Chaer during early cardiac hypertrophy. Silencing Miat expression also suppressed the progression of pathological cardiac hypertrophy both in vitro and in vivo. Transcriptome analysis showed that the ribosome genes were specifically regulated by Miat depletion. Puromycin incorporation assay demonstrated that Miat knockdown substantially reversed the increased protein translation rate upon hypertrophic stimulation. Tagged RNA pull-down and mass spectrum assay identified Nucleophosmin 1 to be the direct target of Miat, which participated in the ribosome assembly process. Taken together, lncRNAs are important factors induced in cardiac hypertrophy to regulate transcription and translation rate, and may serve as novel promising targets in the treatment of clinical heart diseases.

Chunyu Wang – Rensselaer Polytechnic Institute
The transmembrane domain of APP (APPTM) contains the gamma-secretase cleavage site for the release of Abeta.

FAD mutations within APPTM can cause familial Alzheimer's disease by raising Abeta42/Abeta40 ratio. We solved the solution NMR structures of APPTM, in both WT and V44M mutant form and showed FAD mutations can increase the conformational dynamics of a crucial site for Abeta42 production. We also probed the interaction of APPTM with presenilin homologs and found that substrate docking is mediated by juxtamembrane regions, coupled with helical unwinding. Recently, we are carrying out drug discovery for APP-specific inhibitors of gamma-secretase, by screening for binders of APPTM.

Richard Lu – Cincinnati Children's Hospital Medical Center
The heterogeneity of glial subtype progenitors and their malignant counterparts during tumorigenesis has not been fully defined at the single-cell level. Moreover, the relationship between native glial progenitors and pre-cancerous/neoplastic cells, or how distinct glial progenitors constitute and contribute to brain tumorigenesis are not completely understood. Although single-cell RNA-seq analysis of human gliomas has been reported, characterization of murine glial progenitors during development and gliomagenesis at the single-cell level remains incomplete, which impedes modeling and testing strategies to treat brain tumors such as glioblastomas. These unresolved issues impelled us to explore targeted deep-sequencing and intersectional analysis of glial progenitor cells and tumor-forming cells at the single-cell transcriptomic level to identify key determinants of brain tumorigenesis.
To address the heterogeneity of glial progenitors, we performed targeted high-throughput single-cell RNA sequencing (scRNA-seq) on prospective astrocyte lineage cells and OPC populations isolated by fluorescence activated cell sorting (FACS) from neonatal mouse cortices and mapped single-cell expression profiles and molecular features of glial subtype progenitors. We found that astrocyte lineage cells are much more dynamic than previously appreciated and exhibit distinct lineage developmental trajectories in the developing neonatal cortex. Also, our data uncovered an intermediate progenitor population during astrocyte lineage development. In contrast to the astrocyte lineage, the progenitors of oligodendrocytes exhibited a cellular continuum, which included a previously unrecognized primitive OPC subpopulation occurring prior to OPC commitment. Application of scRNA-seq to a murine model of glioblastoma, the most malignant brain tumor, revealed primitive OPCs disproportionately contributing to glioma formation. We also established a new algorithm to identify transcriptional regulator-driven networks and discovered a set of critical transcriptional regulators for glioma growth. Strikingly, signatures of glioma cells closely recapitulated those of transitional glial progenitors during normal development, overrepresenting the more rapidly dividing primitive OPCs in a glioma animal model and human glioma, highlighting possible avenues for selective therapeutic targeting.

Concurrent Session 14: New Investigators Session I

Xu Li – School of Life Science, Westlake University, Shilongshan Road No. 18, Hangzhou, 310024, Zhejiang, China. lixu@westlake

Deciphering the Disease-Related Signaling Pathways Using Functional Proteomics

Sophisticated signaling cascades are required for development and survival. They are highly conserved across species, and control cell growth, proliferation, apoptosis and cell fate. A minor disruption of any of these pathways may cause severe diseases such as cancer. Although the core signaling cascades from ligand binding to transcription activation of downstream genes are well defined, why and how they regulate such diverse physiological and disease outcomes remains unclear.

To understand the global organization of the disease-related signaling pathways and their regulation, here we recruit a variety of cutting-edge proteomics, computational biology and biochemical approaches, to establish protein-protein interaction networks of these pathways. Using such networks, we will be able to explore the network rewiring and understand how it contributes to the pathogenesis. We expect our research will reveal additional insights of the molecular basis of these complicated processes, and shed light on prevention, diagnosis, and treatment of complex diseases.

Keywords: affinity purification; mass spectrometry; interaction network; signaling pathway; phenotype network; disease network; Hippo pathway; Wnt pathway; Notch pathway

Feng Li – Wuhan University College of Medicine

The role of histone demethylase in cancer

The histone methylation\demethylation broadly affects various eukaryotic biological process, such as gene transcription regulation, DNA replication and repair, cell cycle and metabolism. Mutation or overexpression of histone modifying enzymes lead to disease, including cancer. The histone demethylase is frequently overexpressed or mutated in various cancer types, but the underlying mechanism is still not clear. Our work investigated the role histone demethylase in tumorigenesis. We revealed a pivotal relationship between the oncogenic HPV 16E6 proteins expressed by HR HPV isotypes and epigenetic activation of super-enhancers in the genome that drive expression of key oncogenes like EGFR and c-MET. We also identified KDM4B as a novel long interspersed nuclear element-1(LINE-1) regulator and suggested an unexpected oncogenic role of KDM4B overexpression in tumorigenesis, providing clues for the development of new cancer prevention strategies and therapies.

Weibo Luo – UT Southwestern Medical Center

Epigenetic regulation of hypoxia responses in human cancers

Hypoxia is a hallmark of the tumor microenvironment and contributes to tumor malignancy. The transcriptional factor hypoxia-inducible factor (HIF) is a master regulator of response to hypoxia and regulates many hypoxia-induced pathological processes in human cancers, including angiogenesis, metabolism, immune evasion, pH homeostasis, cell survival, maintenance of stem cells, and cell migration/invasion. We recently discovered the epigenetic pathways that surveil HIF activity in human cancers. We found that the epigenetic reader ZMYND8 interacts with the HIF transactivation complex, including HIF-1a HIF-2a and p300, and promotes the transcriptional elongation of the majority of HIF target genes in human breast cancer cells. ZMYND8 is acetylated by p300 and acetylated ZMYND8 recruits BRD4 to the HIF target genes, leading to phosphorylation of RNA polymerase II at serine 2 and gene elongation in human breast cancer cells. ZMYND8 acetylation is necessary and sufficient for breast cancer growth and metastasis in mice. On the other hand, ZMYND8 is upregulated by HIF-1 and HIF-2 in breast cancer cells, thus providing a positive feedback mechanism that amplifies HIF-mediated transactivation in human breast cancer. We also elucidated a negative regulation of HIF-1 transcriptional activity by lysine methylation in human glioblastoma. We found that the lysine methyltransferases G9a and GLP directly bind to HIF-1a and catalyze mono- and di-methylation of HIF-1a at lysine (K) 674 *in vitro* and *in*

vivo. K674 methylation suppresses HIF-1 transcriptional activity and a subset of HIF-1 target genes *PTGS1*, *NDNF*, *SLC6A3*, and *Linc01132* in human glioblastoma U251MG cells. Inhibition of HIF-1 by K674 methylation is mainly caused by reduced HIF-1a transactivation domain function but not increased HIF-1a protein degradation or impaired binding of HIF-1 to hypoxia response elements. K674 methylation significantly decreases HIF-1-dependent migration of U251MG cells under hypoxia. G9a is downregulated by hypoxia in glioblastoma, which is inversely correlated with *PTGS1* expression and survival of patients with glioblastoma. Taken together, our findings uncover the epigenetic mechanisms that maintain high activity of HIF to mediate hypoxia-dependent tumor malignancy in human cancers and yield the possible molecular targets for the treatment of human cancers.

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Wenfei Jin – Southern university of science and technology, China
Comprehensive Mapping of Human Hematopoiesis and Leukemogenesis at Single Cell Resolution
Department of biology, Southern university of science and technology, China
Leukemia is a fatal hematopoietic malignancy, particularly because many patients eventually relapse after effective chemotherapy. Here, we generated >100,000 single-cell transcriptome of bone marrow mononuclear cells (BMMCs) and its subtypes from 4 healthy individuals and 10 leukemia patients. Our analysis showed BMMCs have distinct clusters representing T cells, B cells, monocytes, erythrocytes and so on, while bone marrow CD34+ cells representing hematopoietic stem and progenitor cells showed continuous distribution. We found new cell sub-populations in well-identified cell types, e.g. two megakaryoblast cell populations, two GMP cell populations, three pro-B II cell populations. Especially, we identified new cell lineage and its underlying transcription factors. Analysis of single cell data from leukemia patients showed there are multiple sub-clones among leukemia cells in each patient. We developed a method, composite of multiple tracing statistics (CMTS), that combines tests for multiple lineage tracing approaches, which dramatically increased the accuracy of progenitor inference. Surprisingly, we found progenitors of leukemia cell populations are very diversity and cover many normal cell types. We further found that leukemia cell potentially showed lineage relationship similar to that of normal cells. Thus we hypothesize that stem/progenitor cells with mutated genome will maintain part of its development properties, which lead them developed into a serial of dysfunctional cell populations with corresponding normal cell properties, instead of a homozygous clone. We established a web-based “tumor cells progenitor” pipeline that could accurately identify progenitors of tumor cells based on single cell expression, which could greatly facilitate genetic diagnosis of leukemia. The results and approaches in this study provide the opportunity to develop personalized treatment based on patients’ progenitor of leukemia cells.

Bo Li – UT Southwestern Medical Center
Uncovering the landscape of tumor antigen-specific T cells
Antigen-specific T cells can be orchestrated to kill cancer cells in immunotherapies but the utilities of the TCR information have not been fully explored. Here, we leveraged previously efforts on tumor TCR repertoire, and developed a novel algorithm, iSMART, to characterize antigen-specific TCR clusters. Correlative analysis with gene expression revealed novel regulators for T cell activation. Investigation of single-cell sequencing data revealed a tissue-resident memory signature for selected clonotypes and *ZNF683* as its biomarker. Integrative analysis of TCR clusters with HLA alleles and cancer genomics data identified candidate cancer antigens derived from missense mutations, frameshift indels, and tumor-associated gene overexpression. Predicted antigen *HSFX1* was further validated using vaccinated humanized HLA-A*02:01 mice. Finally, high abundant cancer-associated TCRs were

observed in the blood repertoire of early breast cancer patients, suggesting new avenues for non-invasive early detection. Thus, iSMART-clustered TCRs can identify cancer-associated T cells with broad utilities in immune monitoring and immunotherapies.

Youdong (Jack) Mao – School of Physics and Center for Quantitative Biology, Peking University

A dynamic view on the design principle of human 26S proteasome machinery

The proteasome is an ATP-dependent, 2.5-megadalton machine responsible for selective protein degradation in eukaryotic cells. In this talk, I will summarize our recent studies with cryo-EM on the structures and dynamics of both substrate-free and substrate-engaged human proteasome in a dozen of conformational states at near-atomic resolution. We will discuss how these structures visualize a continuum of dynamic substrate-proteasome interactions from ubiquitin recognition to substrate translocation, during which ATP hydrolysis sequentially navigates through all six ATPases. Most importantly, three principal modes of coordinated hydrolysis are observed, featuring hydrolytic events in two oppositely positioned ATPases, in two adjacent ATPases, and in one ATPase at a time. These hydrolytic modes regulate deubiquitylation, translocation initiation and processive unfolding of substrates, respectively. ATP hydrolysis powers a hinge-like motion in each ATPase that regulates its substrate interaction. Synchronization of ATP binding, ADP release and ATP hydrolysis in three adjacent ATPases drives rigid-body rotations of substrate-bound ATPases that are propagated unidirectionally in the ATPase ring and unfold the substrate. Taken together, these studies reveal how proteasome dynamics elegantly regulate its function as well as the design principle of the proteasome machinery.

Concurrent Session 15: RNA-biology

Wei Chen – SUSTech Academy for Advance and Interdisciplinary Studies
Systematic analysis on *cis*-regulatory code of polyadenylation
Alternative polyadenylation (APA) is widespread across all eukaryotic species, and is recognized as one of the major regulatory mechanisms on gene expression. It can generate transcripts with distinct coding sequence (CDS) and/or 3' untranslated regions (UTR), thereby influencing protein isoforms, mRNA stability and localization. Previous studies have shown that the choice of the polyadenylation site depends on a set of canonical cis sequence features including a prominent hexamer (e.g. AAUAAA) at 10-30nt upstream of cleavage site, the downstream U-rich or GU-rich element and the auxiliary sequences. However, systematical analysis of other cis-regulatory elements is still largely lacking and there is no accurate computational model that can predict PAS usage based on sequence information. Here, I will talk about two ongoing projects. First, I will discuss about the development of a high-throughput screening method to characterize the cis-elements regulating APA. Using this approach, we discovered dozens of novel cis-elements that can modulate PAS usage. Second, I will describe a deep learning architecture that can generate a predicative model to quantify the usage of multiple PAS in an APA-regulated gene. Through a combination of model adjustment and case study, we show how our model can potentially shed light on molecular mechanisms underlying APA regulation.

Yi Xing – University of Pennsylvania School of Medicine
Elucidating alternative isoform variation using massive RNA-seq data
Mammalian cells produce a large number of distinct mRNA and protein isoforms from individual gene loci via alternative processing and modifications of RNA. The recent advent of the high-throughput RNA sequencing (RNA-seq) technology has provided a powerful tool for transcriptome-wide measurements of mRNA isoform complexity at an unprecedented resolution. Large consortium projects have generated RNA-seq data on tens of thousands of samples along with a wide variety of other genomic and phenotypic measurements. However, the use of these large-scale data in routine RNA-seq studies to detect patterns of expression and thereby discover new regulatory events has been limited. In this talk, I will discuss our recent efforts in developing computational and statistical methods for elucidating transcriptome isoform complexity using massive RNA-seq datasets.

Xiaohua Shen – Tsinghua University
Novel functions of RNA-binding proteins in transcription regulation and stem cell pluripotency
Much of the developmental complexity of higher eukaryotes is thought to arise from gene regulation rather than from an increase in the number of protein-coding genes. RNA may represent a hidden layer of regulatory information in complex organisms. Noncoding RNAs have been increasingly recognized as important regulators of transcription and chromatin structure. The fact that RNA-binding proteins (RBPs) must be enlisted to mediate RNA functions raises the possibility that RBPs might participate in transcription control. I will discuss recent progresses we have made in RBP-mediated regulations of gene expression and stem cell pluripotency.

Zhao Zhang – Carnegie Institution for Science
Why piRNAs are needed
Transposons have thrived in the genomes of almost all organisms during evolution. Generating DNA breaks and creating mutations, mobilization of transposons triggers catastrophic genome instability and leads to diseases. In animal gonads, it has been proposed that PIWI-interacting RNAs (piRNAs) suppress transposons to ensure the faithful transmission of genetic information from one generation to the next. However, little is known about whether transposons mobilize in the absence of piRNA protection, and if so, in what cell types. In most studies, transposon activity is typically assessed by the level of

transposon transcripts in whole tissues. In this study, we developed approaches to track transposon mobilization with single cell resolution in live animals, and found that retrotransposons have cell-type specificity for making integration. We discovered that retrotransposons utilize nurse cells, which are highly polyploid (up to 1024C) and eventually undergo programmed cell death during *Drosophila* oogenesis, as factories to massively manufacture invading-products, but rarely transpose back into nurse cells. Instead, via microtubule-mediated transport, retrotransposons preferentially target the DNA of the interconnected oocytes, the only ovarian cells that give rise to the next generation. Notably, blocking microtubule-dependent intercellular transport from nurse cells significantly alleviates damage in the oocyte genome. Our data uncover a novel cell-type specific strategy taken by retrotransposons to maximally propagate in a host genome and highlight the necessity of evolving a specialized small-RNA-based pathway, the piRNA pathway, to shackle them.

Yang Yu – Institute of Biophysics, CAS

A Pandas complex adapted for piRNA-guided transposon silencing

The repression of transposons by the Piwi-interacting RNA (piRNA) pathway is essential to protect animal germ cells. In Drosophila ovaries, Panoramix (Panx) enforces transcriptional silencing by binding to the target-engaged Piwi-piRNA complex, although the precise mechanisms by which this occur remain elusive. Here, we show that Panx functions together with a germline specific paralogue of a nuclear export factor, dNxf2, and its cofactor dNxt1 (p15) as a ternary complex to suppress transposon expression. Structural and functional analysis demonstrate that dNxf2 plays critical roles in Panx association via its UBA domain, and transposon silencing through binding to transposon transcripts directly. Furthermore, dNxf2 interacts with dNxf1 (TAP), which, unexpectedly, is also required for Panx-mediated silencing. Therefore, we propose that dNxf2 may function as a Pandas (Panoramix-dNxf2 dependent TAP silencing) complex, which counteract the canonical RNA exporting machinery (TAP/p15) and restrict transposons within nucleus.

Mofang Liu – Shanghai Institute for Biochemistry and Cell Biology

A Novel Function of LARP7 in Regulating the 2□-O-methylation of U6 snRNA during Spermatogenesis in Mice

U6 snRNA is long known to be highly modified in metazoans, but how U6 modification is regulated still remains less clear. Here, we report that LARP7, a LARP family member that associates with 7SK RNA to function in Pol II regulation, acts as a key regulator for the 2□-O-methylation of U6 in mouse male germ cells. We show that LARP7 associates with box C/D snoRNP in mouse male germ cells and promotes U6 2□-O-methylation by box C/D snoRNP via directly binding to U6 and guide snoRNAs. We further show that LARP7 depletion leads to defective spermatogenesis in mice and a significant reduction of U6 2□-O-methylation in male germ cells. Importantly, transduction of wildtype LARP7, but not a U6 binding-deficient LARP7F38A mutant, is able to functionally rescue U6 2□-O-methylation and defective spermatogenesis in Larp7 mutant mice. Collectively, our findings reveal a novel function of LARP7 in regulating U6 2□-O-methylation and demonstrate that such regulation is essential for spermatogenesis and male infertility in mice.

Concurrent Session 16: Inflammation and autoimmune diseases

Yang Liu, School of Medicine, University of Maryland Baltimore
CD24 and self-nonself discrimination: fundamental concept and translation

Zeng Wenwen. School of Life Science, Tsinghua University
Neural regulation of white adipose tissue plasticity

Li Wu, Tsinghua University School of Medicine
Dendritic cells and macrophages in Immune homeostasis

Bin Li, Shanghai Institute of Immunology, Shanghai Jiaotong University
FOXP3+Treg functional stability and their clinical application

Concurrent Session 17: Stem Cells in Homeostasis and Injury Repair

Qi Zhou – Institute of Zoology, Chinese Academy of Sciences
Progress of stem cell research and translational application in China
In recent years, strategic layouts have been made to support and promote stem cell research in China, including the new round of Chinese Academy of Sciences Strategic Priority Research Program in stem cell research filed that has implemented since late 2017. Original and innovative research on stem cells is encouraged. Regulations and policies on stem cell research and clinical application are being formulated and enacted. Stem cells are categorized as drug for administrative purpose. It is believed that all these will promote great advancement of stem cell research and application in a standardized way in China.
To explore the application potential of stem cells, we have been doing a series of studies in both basic research and in translational applications. We established some new types of stem cells including mouse-rat allodiploid embryonic stem cells and explored their possible application. We performed directed differentiation of stem cells into functional cells, including, for the first time, differentiation of mouse embryonic stem cells into functional haploid sperm cells under completely in vitro conditions. Most recently, we generated bimaternal and bipaternal mice using technologies of haploid stem cells and targeted gene editing.
To promote the clinical application of stem cells, we established Beijing Stem Cell Bank and generated clinical grade stem cells which have been accredited by the National Institutes for Food and Drug Control of China. By transplanting midbrain dopaminergic (DA) neurons derived from a clinical-grade hpESC line into a non-human primate model of Parkinson's disease, we found that the grafts brought variable but apparent behavioral improvement for at least 24 months in most monkeys of experiments and did not form tumors, which provided strong preclinical support for clinical trial. We started the first clinical trials with functional cells derived from clinical grade ECSs, under regulations of National Health and Family Planning Commission and China Food and Drug Administration, to treat Parkinson's disease and age-related macular degeneration. The first group-standard on stem cells in China, "General Requirements for Stem Cells", has been published, which will play an important role in promoting regulatory stem cell research and application in China.

Hongkui Deng – College of Life Sciences and Peking-Tsinghua Center for Life Sciences
Small molecules induced cell reprogram

Xiaoqun Wang – Institute of Biophysics Chinese Academy of Sciences
Neural stem cell subtypes and cortical development

Zhenguo Wu – the Hong Kong University of Science and Technology
Regulation of quiescence exit in muscle stem cells
Adult mouse muscle satellite cells (MuSCs) are quiescent in uninjured muscles. Upon injury, MuSCs exit quiescence to become activated, re-enter the cell cycle to proliferate, then differentiate to repair the damaged muscles. It remains unclear which extrinsic signal and intrinsic signaling pathway regulate quiescence exit during MuSC activation. Here, we demonstrated that inducible MuSC-specific deletion of p110α, a catalytic subunit of phosphatidylinositol 3-kinase (PI3K), rendered MuSCs unable to exit quiescence, resulting in severely impaired MuSC proliferation and muscle regeneration. Genetic reactivation of mTORC1, or knockdown of FoxOs, in p110α-null MuSCs partially rescued the above defects, making them key effectors downstream of PI3K in regulating quiescence exit. Jun was found to be a key transcriptional target of the PI3K/mTORC1 signaling axis essential for MuSC to exit quiescence. Moreover, induction of a constitutively active PI3K in quiescent MuSCs resulted in spontaneous MuSC activation in uninjured muscles and subsequent depletion of the MuSC pool. Thus, PI3K is both necessary and sufficient for MuSCs to exit quiescence in response to activating signals.
(This work was supported by research grants from the Hong Kong Research Grant Council

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Jingsong Li – Institute of Biochemistry and Cell Biology, CAS

Artificial sperm mediated gene editing

From androgenetic haploid blastocysts derived by injection of sperm into enucleated oocytes, we generate mouse androgenetic haploid embryonic stem cells (AG-haESCs) that can support full-term embryonic development upon injection into oocytes, leading to the generation of semi-cloned (SC) mice (semi-cloned technology)[1]. However, one major drawback of this technology is the very low birth rate of healthy SC mice (2% of total SC embryos). Recently, we establish AG-haESCs carrying H19-DMR and IG-DMR deletions (DKO-AG-haESCs) that can efficiently support the generation of SC pups at a rate of 20% ("artificial sperm")[2]. Importantly, "artificial sperm"carrying CRISPR-Cas9 library can produce biallelic mutant mice in one step, thus enabling functional mutagenic screening at organism level in mice[2]. Moreover, artificial sperm-mediated SC technology enables efficient generation of mouse models carrying defined point mutation[3]; one-step generation mouse models that mimic multiple gene dosage effect in human Myotonic Dystrophy type 1 (DM1); identification of novel mutations involved in human neural tube defects; medium-scale targeted screening of critical factors involved in bone development; and efficient generation of mice carrying tagged proteins at genome-scale (genome tagging project, GTP). Interestingly, we demonstrated that parthenogenetic haESCs derived from oocytes, after removing H19-DMR and IG-DMR, can also support the high-efficient generation of SC mice by injection into oocytes, thus enabling high-efficiency bi-maternal development in mammals[4]. Furthermore, we establish haploid ESCs from monkey parthenogenetic embryos[5] and human parthenogenetic haESCs[6]. In summary, haESCs provide powerful tools for genetic analyses in mammals at both the cellular and organismal levels[7].

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Daunqing Pei – Guangzhou Institutes of Biomedicine and Health, CAS

Single-cell analysis of three reprogramming systems reveals a generic model for cell fate transitions

The conversion of a somatic cell to pluripotent ones by Oct4, Sox2, Klf4 and Myc, i.e., the Yamanaka factors, is a breakthrough for basic biology. This reprogramming approach has generated insights into how cell fate transitions are regulated, including the identification of intermediates with distinct molecular signatures, and mechanisms regulating mesenchymal-to-epithelial transition (MET), histone and DNA demethylations, all based on bulk studies. Yet, as only a small fraction of the starting cells become pluripotent, a single cell approach is needed to define general principles of reprogramming. Here we map the fate continuum generated by Yamanaka, chemical or a new seven-factor system at single-cell resolution. In all three systems, certain cells acquire pluripotency via a reprogramming potential (RP) trajectory, many others bifurcate at various stages into non-reprograming (NR) branches dependent on culture conditions and factors employed. NR fates are marked by *Cd34*+/*Fxyd5*+/*Psca*+, *Dcn*+/*Cdkn2a*+ and *Sox17*+/*H19*+, and *Ins2*+ and *Cdh2*+/*Sall4*+/*Oct4*- in three systems respectively. Focusing on *Oct4*/*Sox2*/*Klf4* system, we show that Klf4 is responsible for the *Cd34*+/*Fxyd5*+/*Psca*+ NR fate which can be antagonized by Sox2. Our work reveals a generic bifurcation model for cell fate transition during reprogramming, implying that NR may be minimized in order to improve

reprograming. More broadly, this cell fate model may be applicable to cell specification in development or cancer.

Concurrent Session 18: Infection and Host Defense

Xing Chang – Shanghai Institutes of Biological Sciences, Chinese Academy of Sciences, Shanghai, China.

Regulation and manipulation of RNA processing in the immune system

Posttranscriptional regulation is mediated through multiple steps of mRNA processing, including alternative splicing of pre-mRNA, 3'UTR regulation, and translational control, all typically mediated through interactions between RNA-binding proteins (RBPs) and their target sequences on RNA. *First,* to gain insight into posttranscriptional regulation in T cells, we have identified that PCBP1, an RNA binding protein with iron chaperon activity, is able to sense iron to promote proinflammatory cytokine expression. Our data indicate a mechanism by which iron deposition promotes tissue inflammation, representing a simple yet effective means of adjusting the inflammatory response in response to iron metabolism, a critical process in normal tissue homeostasis. *Second,* we have developed a genetic approach to efficiently modulate RNA splicing in their native chromatin context. Based on our previously developed CRISPR-guided cytidine deaminase, this approach precisely edits universal cis-regulatory elements of splicing to either suppress or promote inclusion of an exon, enabling both loss-of-function and gain-of-function analysis using the same platform. We further demonstrate that this method is able to dissect splicing codes and correct aberrant splicing associated with genetic diseases.

Shan-Lu Liu – The Ohio State University, Viruses and Emerging Pathogens Program and Center for Retrovirus Research, 1900 Coffey Road, Columbus, OH

Restriction of HIV infection by TIMs and viral antagonism lentivirus Nef

HIV infection is known to be restricted by numerous cellular factors, yet the virus has evolved many mechanisms to counteract them. We recently reported that the T cell immunoglobulin and mucin domain (TIM) proteins inhibit release of HIV-1 and other enveloped viruses by interacting with cell- and virion-associated phosphatidylserine (PS). Here, we provide evidence that the Nef proteins of HIV-1 and other lentiviruses antagonize TIM-mediated restriction of viral release in part through SERINCs. TIM-1 more potently inhibits the release of Nef-deficient relative to Nef-expressing HIV-1, and ectopic expression of Nef, or knockdown of TIM proteins, relieves this restriction. SERINC3 or SEERINC5 potentiates the inhibitory effect of TIM-1 on HIV-1 release, especially that of Nef-deficient viruses. Conversely, depletion of SERINC3 or SERINC5 proteins attenuates TIM-mediated restriction of HIV-1 release. Biochemical and imaging assays show that SERINCs stabilize the expression of TIMs in the cell and that HIV-1 Nef proteins downregulate both SERINCs and TIMs. Consistent with this model, MLV glycoGag and EIAV S2 proteins, which are known to counteract SERINCs, also effectively counteract TIM-mediated inhibition of HIV-1 release. Collectively, our work reveals a complex interplay between lentiviral Nef proteins and cellular restriction of HIV by TIMs and SERINCs.

Qi-Jing Li – Duke University School of Medicine

Tumor as a Suppressive Immune Organ

By 2013, the unprecedented success of anti-PD1 therapy against various solid tumors terminated the long-standing debate whether the human immune system can recognize and eradicate tumors. Accordingly, it is well appreciated that the tumor microenvironment utilizes multiple mechanisms to suppress immune responses locally. Clinically, opportunistic infection is one of major complications leading to morbidity and mortality especially at terminal stages of cancer patients; and, these patients generally have deficiency to mount an effective vaccine response. However, the global impact or of an established tumor on the immune system is understudied and its mechanisms remains elusive. Through immunogenomics studies on mouse tumor models, we revealed complex interplays between tumor and the host immune system. Novel innate and adaptive cell lineages were discovered and trans-differentiation pathways were identified. Overall, these studies illustrate that as a pathologically developed "organ", established tumors have the capacity to

reprogram the entire immunity towards a systemic suppression.

Yisong Wan – The University of North Carolina at Chapel Hill, 125 Mason Farm Rd, Chapel Hill, NC

The control of helper T cell generation and function in inflammation and disease

CD4 Helper T (Th) cells are critically involved in health and diseases including immune homeostasis, pathogen clearance, autoimmunity, inflammation and cancer. How Th cells are differentiated and how the functions of Th cells are controlled are under intensive investigation in recent years. Depending on the cytokines provided, Th cells can be generated with either immune regulatory or pathogenic functions. We are interested in investigating the molecular mechanisms underlying Th cell generation and function. Among Th cell subsets, Th17 cells are of particular interest, as they have broad function relevant to diverse immune diseases. In this presentation, I will discuss our recent findings related to how TGF-beta signal promotes Th17 cell differentiation and a novel pathway that directs pathogenic Th17 cell generation in inflammation and disease.

Qiming Liang– Shanghai Institute of Immunology, Shanghai Jiao Tong University School of Medicine

Virus-host interactome reveals the unique blockage of host RNAi machinery by Zika virus

The recent outbreaks of Zika virus (ZIKV) and its association with birth defects known as Congenital Zika Syndrome warrant investigation on the molecular processes related to its infection and pathogenesis. Among the flavivirus family, only ZIKV is linked to microcephaly as announced by World Health Organization, suggesting uniqueness of ZIKV infection compared to other members. By analyzing the ZIKV-host interactome, we found that the key microRNA processing protein DICER was the top target of ZIKV capsid protein in neural stem cells (NSCs), and its deficiency facilitated ZIKV infection. Mechanistically, ZIKV capsid can directly interact with DICER and block its ribonuclease activity, dampening the production of both viral interfering RNAs and host microRNAs that are essential for neurogenesis. Interestingly, this capsid-mediated immune evasion is specific to ZIKV because capsid proteins from other close flaviviruses, e.g., dengue, yellow fever and West Nile viruses, cannot bind to DICER or inhibit its function. Thus, our study demonstrated that capsid-dependent suppression of DICER function is a unique determinant of ZIKV immune evasion and pathogenesis, which may unveil a new mechanism for ZIKV-mediated microcephaly.

Jixi Li – Huashan Hospital, Fudan University

Structural basis of cell necrosis and its implications in neurodegenerative diseases

The RIP1/RIP3 necrosome is an amyloid signaling complex that initiates TNF-induced necroptosis, serving in human immune defense, cancer and neurodegenerative diseases. RIP1 and RIP3 associate through their RIP homotypic interaction motifs. We identified RIP1/RIP3 forms a functional amyloid complex in cell necroptosis (2012, Cell). Recently, we solved the high-resolution structures of the RIP1-RIP3 core by using ssNMR and X-ray crystallography methods (2018, Cell). RIP1 and RIP3 alternately stack to form heterotypic β-sheets. Two such β-sheets bind together to along a compact hydrophobic interface featuring an unusual ladder of alternating Ser (from RIP1) and Cys (from RIP3). The RIP1/RIP3 core is the first detailed structure of a hetero-amyloid, and provides a potential explanation for the specificity of hetero- over homo-amyloid formation and a structural basis for understanding the mechanisms of signal transduction. Moreover, our current data show that the RIP1/RIP3 necrosome is involved in neurodegenerative diseases, including AD and ALS.

Concurrent Session 19: Tumor Microenvironment and Metastasis

Erwei Song, Sun Yat-sen University, Guangzhou, China
Treat the cancer soil: Turn foes to friends
Current paradigms of cancer-centric therapeutics are usually not sufficient to eradicate the malignancy, while cancer stroma may prompt tumor relapse and therapeutic resistance. Among all the stromal cells that populate the tumor microenvironment, tumor-associated macrophages (TAMs), cancer-associated fibroblasts (CAFs) and tumor-infiltrated lymphocytes (TILs) are the most abundant and are critically involved in cancer progression. Tumor stromal cells regulate the biology of tumor cells via cell-cell contact, numerous regulatory factors and synthesizing or remodeling the extracellular matrix, and thus affect cancer initiation and development. Therefore, recent characterization of tumor microenvironment brings stroma-targeting therapies for cancer treatment onto the agenda. In our studies, we not only underscore the contribution of tumor stroma components to cancer progression, but also highlight the relevant translational advances and potential therapeutic strategies that target tumor soil for cancer treatment.

Li Ma – The University of Texas MD Anderson Cancer Center
A lncRNA saga in metastasis
A paradigm-shifting 6-year study from my lab unearthed the unexpected metastasis-suppressing function of the lncRNA MALAT1 through highly rigorous genetics approaches—comprehensive targeted inactivation, restoration (genetic rescue), and overexpression approaches in genetically engineered mouse models, xenograft models, and syngeneic models; and revealed a novel mechanism by which MALAT1 lncRNA sequesters and inactivates the pro-metastatic transcription factor TEAD to suppress metastasis. Our findings defy the conclusions drawn from previous MALAT1 genomic deletion (which caused upregulation of 12 genes adjacent to MALAT1) and antisense RNA studies that lacked rescue experiments, call for rectification of the model for a highly abundant and conserved lncRNA, and provide the general framework for rigorous characterization of lncRNAs.

Bin Zhou– Shanghai Institutes for Biological Sciences
Fate mapping of epithelial-to-mesenchymal transition for tumor metastasis
Unraveling cell fate transitions or switches provide fundamental information to understand tissue regeneration and diseases. Certain types of cell fate switch are reversible and transient, whereby one cell can switch to an alternative state and then switch back again shortly, such as epithelial-to-mesenchymal transition (EMT) in tumor cells. Due to its transient nature, tracking EMT in vivo remains challenging, and there is no clear genetic tracing evidence of EMT for tumor metastasis so far. Here we generated a dual recombinases-mediated tracing system that permits induced seamless tracking of transient cell fate switch. By spontaneous breast-to-lung tumor metastasis model, this new system traced the transient EMT occuring from primary tumor to distant metastatic sites, providing in vivo genetic evidence of EMT for tumor metastasis. This system would be valuable for broadly studying transient cell fate switch in tissue regeneration and diseases.

Jing Yang - Department of Pharmacology, Moores Cancer Center, University of California, San Diego, La Jolla, CA USA
Epithelial-Mesenchymal Plasticity in Carcinoma Metastasis
During metastasis, epithelial tumor cells dissociate from each other, disseminate into the systemic circulation, and then establish secondary tumors in distant sites. A developmental program termed Epithelial-Mesenchymal Transition (EMT) is implicated in promoting the dissemination of single carcinoma cells during metastasis. Both the Twist and Snail families of transcription factors are key inducers of EMT and tumor metastasis. Using an inducible Twist1 mouse model, we show that activation of Twist1 is sufficient to promote carcinoma cells to undergo EMT and disseminate into blood circulation. Importantly, in distant sites, turning off Twist1 to allow reversion of EMT is essential for disseminated tumor cells to

proliferate and form macrometastases. These data indicate that EMT is dynamically regulated during tumor metastasis: carcinoma cells undergo EMT to disseminate; once reaching distant site, they need to revert to an epithelial identity to form macrometastases. I will also present our ongoing studies that aim to understand how EMT is dynamically regulated in response to signals from the tumor microenvironment and from the intracellular machineries to impact EMT and tumor metastasis.

Guohong Hu - Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences, 320 Yueyang Road, Shanghai, China

Regulation of breast cancer metastasis organotropism

Cancer metastasis is a major obstacle for cancer therapeutics, and organotropism is an important feature of cancer distant metastasis. But the regulatory mechanism of metastasis organotropism remains unclear. Here we show that the WNT antagonist DKK1 with dichotomous roles in breast cancer metastasis to lungs and bone. DKK1 expression is down- and up-regulated, respectively, in lung- and bone-metastatic breast cancer cells, as well as in clinical samples. Functionally tumor-secreted DKK1 suppresses lung colonization while promotes osteolytic metastasis of breast cancer, by regulating different WNT downstream signaling and different stromal components in the organs. Therefore, our data highlight the roles of WNT signaling and tumor microenvironment in organotropic metastasis, and provide a rationale for new approaches to treat systemic metastasis.

Concurrent Session 20: Epigenetic Regulation

Haitao Li – Tsinghua University
Hierarchical Histone Deacetylation by Sirtuins
Chemical modifications on histones constitute a key mechanism for gene regulation in chromatin context. Besides acetylation, a repertoire of non-acetyl histone acylations has been identified, such as formylation, propionylation, butyrylation, crotonylation, succinylation, glutarylation, 2-hydroxyisobutyrylation, and β-hydroxybutyrylation. The sirtuin family proteins (e.g. human SIRT1-7) are a class of NAD-dependent deacetylases that remove acyl marks from various cellular proteins including histones. In particular, histone lysine β-hydroxybutyrylation (Kbhb) was identified as a new form of histone acylation that connects starvation-responsive metabolism to epigenetic regulation. Through systematic profiling studies, we showed that human SIRT3 functions as a histone de-β-hydroxybutyrylase with site preferences for H3 K4, K9, K18, K23, K27, and H4K16. Interestingly, SIRT3 is incapable of removing bhb at sites H4 K5, K8, K12 that have flanking glycine residues both in vitro and in cells. Such a unique class-selectivity is not observed in HDAC3, a key member of the Zn-dependent histone deacetylases. Structural studies revealed a hydrogen bond-lined hydrophobic pocket favored for the S-form Kbhb recognition and catalysis. β-backbone but not side chain-mediated interactions around Kbhb dominate sequence motif recognition, explaining the relatively broad site-specificity of SIRT3. The observed class-selectivity against sites like H4K8 is due to the intrinsic flexibility of the glycine-flanking motif they reside in. Collectively, we revealed the molecular basis for class-selective histone deacylation by SIRT3, shedding new lights on the function of sirtuins in through hierarchical deacylation.

Cheng-Ming Chiang – UT Southwestern
BRD4 in Transcription Programming and Cancer Therapy
Bromodomain-containing protein 4 (BRD4) is an epigenetic regulator and transcription cofactor whose phosphorylation by casein kinase II (CK2) and dephosphorylation by protein phosphatase 2A (PP2A) modulates its function in gene-specific targeting and recruitment of transcriptional regulators and chromatin modifiers. Although BRD4 has emerged as an important cancer therapeutic target, it also plays crucial roles in diverse cellular processes, including cell cycle progression, DNA damage response, chromatin structure maintenance, stem cell reprogramming, cell lineage differentiation, X-chromosome inactivation, and viral latency and reactivation. While the bromodomains of BET family proteins including BRD4, BRD2, BRD3 and BRDT have been the primary targets of small compounds, such as JQ1 and I-BET, that show promising anticancer effects against some hematopoietic cancer and solid tumors, the issue related to drug resistance upon prolonged treatment necessitates a better understanding of alternative pathways underlying not only the resistance but also persistent BET protein dependence. In our studies of BRD4 phosphorylation, we identified three dozen small compound inhibitors targeting phosphorylation-dependent BRD4 interactions with distinct transcription/replication factors including p53, c-Myc, AP-1, and cancerassociated human papillomavirus (HPV) E2 proteins. Some of these identified phospho-BRD4-targeting compounds effectively block cancer cell growth and migration and specifically inhibit p53 interaction with BRD4, but not BRD2 and BRD3, highlighting the development of a new class of BRD4-specific inhibitors without crossinterference with the other BET family proteins. Intriguingly, certain phospho-BRD4 compound inhibitors exhibit target selectivity to only the oncogenic but not the tumorsuppressive activity of BRD4, with outcomes significantly different from the widely used JQ1- and I-BET-derived BET bromodomain inhibitors.

Yanming Wang – School of Life Sciences, Henan University
Histone hypercitrullination in autoimmunity and cancer metastasis
Histone hypercitrullination was found to play a critical role in a novel form of cell death called netosis, wherein neutrophils extrude its chromatin fibers into extracellular space. Without

the conversation of arginine residues to citrulline in histone proteins via the peptidylarginine deiminase 4 (PAD4/PADI4) enzyme, netosis will not occur. Importantly, unrestricted netosis under inflammatory conditions or within the tumor microenvironment underlies the pathological development of a range of diseases, including cancer progression, metastasis, rheumatoid arthritis, ischemia/reperfusion injury, thrombosis, etc. As such, PAD4/PADI4 is now on the radar screen for drug development and targeted therapy by biotech companies and big pharma. I will talk our current understanding of the role of PAD4 in chromatin structure regulation during netosis and its involvement in cancer immunobiology.

Gang Wang – Shanghai Institutes of Biological Sciences, CAS
Zhi-Chao Wang, Dan Cao, and Gang Wang – Inst of Biochem & Cell Biol, Chinese Academy of Sciences,
Mediator-ing transcription and epigenetics in liver diseases
Liver fibrosis is characterized by persistent accumulation of extracellular matrix components that is often associated with high risk of cirrhosis and hepatocellular carcinomas, though the underlying molecular mechanisms are largely unknown. Here we show that transcriptional cofactor Mediator Med23 subunit is involved in experimental liver fibrosis. Mice with hepatic *Med23* ablation exhibit aggravated carbon tetrachloride-induced liver fibrosis, with enhanced chemokine expression and liver inflammatory infiltration, as well as improved hepatocytes regeneration compared with control littermates. Mechanistically, we identified an orphan nuclear receptor RORa as an upstream activator for Ccl5 and Cxcl10 expression, which is suppressed by liver MED23. Furthermore, the negative effects of Med23 for Ccl5 and Cxcl10 are possibly due to increased G9a-mediated H3K9 dimethylation at the target gene promoters. Collectively, our data revealed hepatic Mediator Med23 as a key suppressor of liver fibrosis, and modulation of the MED23-Ccl5/Cxcl10 axis may provide possible intervening strategies for liver fibrosis.

Xiaoling Li – National Institute of Environmental Health Sciences
Metabolic and Epigenetic Regulation of Embryonic Stem Cell Maintenance and Differentiation
The developing embryos require a number of indispensable nutrients to support rapid cell division during the early stages of fetal development. In particular, embryonic stem cells (ESCs) derived from the inner cell mass of a blastocyst have a high dependence on methionine metabolism for epigenetic and redox homeostasis and maintenance of pluripotency compared to differentiated cells. However, remarkably, little is known about the regulation of cellular methionine metabolism. Through global metabolomics, functional metabolic analysis, epigenetic profiling, and *in vivo* mouse studies, we recently discovered that the SIRT1, a highly conserved NAD^+-dependent protein deacylase, is a novel regulatory factor for cellular methionine metabolism and histone methylation. We showed that SIRT1 deficient mESCs are hypersensitive to methionine restriction-induced differentiation and apoptosis, primarily due to a reduced conversion of methionine to S-adenosylmethionine. This reduction markedly decreases methylation levels of histones, resulting in dramatic alterations of gene expression profiles. Mechanistically, we found that the enzyme converting methionine to S-adenosylmethionine in mESCs, methionine adenosyltransferase 2a (MAT2a), is under control of Myc and SIRT1. Importantly, SIRT1 KO embryos display reduced *Mat2a* expression and histone methylation, and are sensitive to maternal methionine restriction-induced lethality, whereas maternal methionine supplementation increases the survival of SIRT1 KO newborn mice. Our findings uncover a novel regulatory mechanism for cellular methionine metabolism, and highlight the importance of methionine metabolism in SIRT1-mediated mESC maintenance and embryonic development.

Greg G Wang – University of North Carolina Chapel Hill
DNMT3A, CpG vs non-CpG methylation, and human disease

Concurrent Session 21: Genome Maintenance

Zhenkun Lou - Mayo Clinic
Regulation of DNA-Protein Crosslinks
Covalent DNA-protein crosslinks (DPCs) are toxic DNA lesions that interfere with essential chromatin transactions, such as replication and transcription. Recent data has shown that DPC repair by SPRTN is essential for the maintenance of genome stability, and hypomorphic mutations in SPRTN cause premature ageing and tumorigenesis in mice and humans. Therefore, exploring the DPC pathway by SPRTN will be paramount to understanding the complex signaling mechanisms orchestrating DPC repair.
SPRTN, a DNA-dependent metalloprotease, is a central player in DPC repair. SPRTN cleaves various DNA binding substrates during S-phase progression and thus protects human proliferative cells from DPC toxicity. The ubiquitin switch is the most upstream regulatory mechanism of SPRTN in DPC repair, but the mechanism underlying this modification is still largely unknown. Here we found a new deubiquitinase that regulates SPRTN deubiquitination and activation upon DPCs.

Junran Zhang –The Ohio State University
Identifying New Biomarkers to Guide the Use of Cell Cycle Checkpoint Inhibitors
The cell cycle checkpoint proteins ataxia-telangiectasia-mutated-and-Rad3-related kinase (ATR) and its major downstream effector checkpoint kinase 1 (CHK1) prevent the entry of cells with damaged or incompletely replicated DNA into mitosis when the cells are challenged by DNA damaging agents, such as radiation therapy or chemotherapeutic drugs. This regulation is particularly evident in cells with a defective G1 checkpoint, a common feature of cancer cells, due to p53 mutations. In addition, ATR and/or CHK1 suppress replication stress by inhibiting excess origin firing, particularly in cells with activated oncogenes. Those functions of ATR and CHK1 make them ideal therapeutic targets. ATR and CHK1 inhibitors have been developed and are currently used either as single agents or paired with radiotherapy or a variety of genotoxic chemotherapies in preclinical and clinical studies. However, to date only limited efficacy has been noted in clinical trials. Originally, p53 was thought to be a biomarker predictive of response to CHK1 inhibitors when combined with radiotherapy and chemotherapy; however, a clinical study suggested that p53 status was not associated with treatment outcome with CHK1 inhibitors. More recent preclinical studies suggest that ATR and CHK1 inhibitors can be used as single agents to target cancer cells with a high level of replication stress. The discovery of new biomarkers to guide the use of these agents will significantly improve their efficacy. In this presentation, I will provide the evidence to support the role of RNF126 in guiding the use of ATR and CHK1 inhibitors and discuss the possibility to identify new biomarkers predictive of response to ATR and CHK1 inhibitors by a high-throughput Decode Pooled shRNA screen.

Zhongsheng You – Washington University School of Medicine
Genome maintenance: signaling through Ca2+
A major source of mutation and genomic instability in cancer is DNA replication. The progression of the replication fork can be impeded by many factors including insufficient nucleotides, DNA lesions, secondary structures and collisions with the transcription machinery. These challenges necessitate mechanisms in cells that preserve stalled fork structure so that replication can restart and complete after the removal of the stress. The ATR-Chk1 checkpoint and a number of fork-associated factors such as BRCA1, BRCA2, FANCD2, BOD1L, RAD51 and CtIP have been shown to play a crucial role in fork protection after replication stress. Here we report a new fork protection pathway, which acts to restrain the activity of the exonuclease Exo1 to prevent aberrant fork processing that otherwise could cause fork collapse and DNA damage. Our results suggest that replication stress elevates intracellular Ca^{2+} levels, leading to the activation of CaMKK2 and the downstream kinase AMPK. Following activation, AMPK directly phosphorylates Exo1 to prevent its association with stressed replication forks, thereby avoiding deleterious fork processing. Disruption of

this pathway results in excessive fork degradation, chromosomal instability and hypersensitivity to replication stress inducers. This finding reveals a novel link between calcium signaling and genome maintenance during DNA replication, and may have implications for tumorigenesis and cancer treatment.

Xingzhi Xu – Shenzhen University
MRN UFMylation promotes ATM activation
A proper DNA damage response (DDR) is essential to maintain genome integrity and prevent tumorigenesis. DNA double-strand breaks (DSBs) are the most toxic DNA lesion and their repair is orchestrated by the ATM kinase. ATM is activated via the MRE11-RAD50-NBS1 (MRN) complex and its autophosphorylation at S1981 and acetylation at K3106. Activated ATM rapidly phosphorylates a vast number of substrates in local chromatin, providing a scaffold for assembly of higher-order complexes that can repair damaged DNA. While reversible ubiquitination has an important role in the DSB response, modification of the newly identified ubiquitin-like protein (UBL) UFM1 and the function of UFMylation in the DDR is largely unknown. Here, we found that MRE11 is UFMylated on one lysine residue and this UFMylation is required for optimal ATM activation, homologous recombination-mediated DSB repair and genome integrity. A pathogenic mutation MRE11(GC) identified in uterine endometrioid carcinoma exhibited a similar cellular phenotype as a UFMylation-defective mutant MRE11(KR). Taken together, MRE11 UFMylation promotes ATM activation, DSB repair, and genome stability and potentially serves as a therapeutic target.

Weihang Chai – Washington State University School of Medicine
Regulation of replication fork stability by ssDNA-binding proteins
Fragile sites (FSs) are chromosomal loci that are prone to breakage upon replication stress (RS), and are thought to represent difficult-to-replicate genomic regions. Telomeres, the ends of chromosomes formed by tandem TTAGGG repeats and abundant telomere-binding proteins, are sensitive to replications stress and are considered as FSs. FS instability is presumably caused by the collapse of stalled replication forks at or near these loci, which generates DNA strand breaks that can lead to unwanted repair/rearrangement activities, driving genome instability. FS instability has been associated with pathological diseases including complex diseases and cancer. To preserve genome stability, cells have evolved a plethora of proteins to prevent fork stalling at FSs and to facilitate the restart of stalled replication.
The RPA-like ssDNA binding protein complex CTC1/STN1/TEN1 (CST) is a conserved telomere maintenance factor. It promotes efficient replication of telomeric DNA and is also important for promoting the stability of GC-rich and repetitive fragile sequences genome-wide under RS. We have shown that CST deficiency leads to spontaneous chromosome breakage and high-level chromosome fragmentation that can be further exacerbated by RS. Upon fork stalling, CST proteins form distinct nuclear foci that colocalize with RAD51. Furthermore, RS induces physical association between CST with RAD51. CST deficiency diminishes HU-induced RAD51 foci formation and reduces RAD51 recruitment to GC-rich fragile sequences and telomeres. Our findings establish that CST promotes RAD51 recruitment to stalled sites to facilitate replication restart. Pathogenic CST mutations identified from Coats plus, a rare complex genetic disease characterized by multi-system disorder, cause both telomere dysfunction and chromosome instability, suggesting that the molecular basis of Coats plus pathology is genome and telomere instabilities driven by replication defects.
We will also discuss our most recent findings on mapping and profiling of FSs induced by various replication stressors genome-wide.

Zhiyuan Shen, Rutgers Cancer Institute of New Jersey, Rutgers University
Genomic signatures of tumors initiated by BCCIP deficiency.
Defects of caretaker genes often lead to a genomic instability that drives tumorigenesis by causing secondary genomic alternations of gatekeeper tumor suppressors or driver

oncogenes. The spectra of these gatekeeper mutations are often associated with the cancer types. Cancer genomes also have complex spectra of passenger mutations and structural variations that reflect the underlining defect of a specific genome maintenance pathway. A well-known example is the genome-wide microsatellite instability that is not necessary a direct driver of tumorigenesis but a genome signature for a defect in the DNA mismatch repair pathway. Establishment of genome structural signature resulted from defect of distinct DNA repair pathway may offer the means to identify the DNA repair defect in the tumors without the need to know the specific genes involved.

BCCIPβ is a revolutionary conserved protein. Both mammalian and Ustilago maydis BCCIPβ interacts with a highly conserved domain of the BRCA2 protein. To derive a genomic signature of tumors initiated from BCCIP defect, we analyzed the genome of medulloblastomas that were initiated by transient Bccip down-regulation in mice. We found that, in addition to excessive chromosome translocations that can be caused by defective DNA double strand break repair, these tumors often have a signature of Bridge-Fusion-Break that can be caused by cleavage of anaphase chromosome bridges. These analyses suggest that BCCIP defects contribute to tumorigenesis due to a defective DNA double strand break repair and BCCIP may also have a function in DNA replication fork stability.

Concurrent Session 22: Structural Biology

Xuewu Zhang – University of Texas Southwestern Medical Center at Dallas
Transmembrane signaling mechanisms of plexin
The research of our lab is focused on mechanisms of transmembrane signaling of plexin. Plexins are cell surface receptors for semaphorins, the largest family of neuronal axon guidance molecules. Signals through the semaphorin/plexin pathways not only play critical roles in neuronal development, but also regulate other processes such as angiogenesis and immunity. In the past, we have demonstrated that the plexin intracellular region transduces signal by acting as a non-canonical GAP for the small GTPase Rap, instead of the previously reported R-Ras and M-Ras. We elucidated the autoinhibition and the activation mechanisms of plexin by determining its structure in different states. We have also worked out how plexin interacts with various intracellular regulators and transducers. Our structural analyses of plexin interacting with two different PDZ-containing proteins suggested that 3-dimensional domain mediated interactions provide an additional affinity/specificity enhancer for PDZ/target interactions. Our work also revealed how the adaptor protein GIPC1 and the motor protein myosin VI together form large oligomeric complexes with PlexinD1 to mediate its endocytic transport. More recently, we have started using Cryo-electron microscopy to analyze how the transmembrane region in plexin couples the extracellular and intracellular domains to allow precise control of plexin signaling in response to binding of the semaphorin ligand to the extracellular region.

Weikai Li – Washington University at St. Louis
Structure basis of anticoagulation with vitamin K antagonization
Vitamin K antagonists (VKAs) are among the most commonly used drugs worldwide. These anticoagulants inhibit the intramembrane vitamin K epoxide reductase (VKOR) to prevent blood clotting. Using live-cell mass spectrometry based footprinting, we have elucidated the native folding topology of human VKOR and captured an electron-transfer process that maintains the VKOR activity in the cellular environment. We have also determined eleven crystal structures of human VKOR and a VKOR-like paralog with VKAs and substrates in different redox states. The structures reveal that VKOR catalysis starts from a partially oxidized state, which affords a reactive cysteine to form a substrate adduct. This stable adduct induces a structural conversion to enable electron transfer that drives catalysis. The catalysis requires keto–enol tautomerism of vitamin K, mediated by the same key residues recognized by VKAs. Bound VKAs locks VKORs into a close conformation, whereas the catalytic cycle requires these enzymes to close for substrate reduction and to open for product release. This difference is the key to the VKOR catalysis and vitamin K antagonism.

Xinzheng Zhang – Institute of Biophysics - CAS
Near-atomic structure of PBCV-1, a nucleo-cytoplasmic large dsDNA virus
Although the Nucleo-Cytoplasmic Large DNA Viruses (NCLDVs) are one of the largest group of viruses that infect many eukaryotic hosts. High-resolution structures of these viruses have been lacking. Many of these viruses have approximate icosahedral capsids. Here we report the 3.5 Å resolution capsid structure of Paramecium bursaria chlorella virus 1 (PBCV-1). The structure consists of ~5040 copies of the major capsid protein. ~60 copies of the penton protein and 1800 minor capsid proteins of which there are 13 different types. The minor capsid proteins form a hexagonal network below the outer capsid shell, stabilizing the capsid by gluing neighboring capsomers together. The size of the viral capsid is determined by about 60 copies of a “tape measure protein”, one of the minor capsid proteins. Homologs of the tape-measure protein and some of the other minor capsid proteins exist in other NCLDVs. Thus a similar capsid assembly pathway might be used by other NCLDVs.

Beili Wu – Shanghai Institute of Materia Medica - CAS
Structural basis of signal recognition and regulation at the full-length glucagon receptor

The human glucagon receptor (GCGR) belongs to the class B G protein-coupled receptor (GPCR) family and plays a key role in glucose homeostasis and the pathophysiology of type 2 diabetes. Here we report two crystal structures of full-length GCGR containing both extracellular domain (ECD) and transmembrane domain (TMD) at different coformational states. Notably, the stalk region, which connets the ECD and TMD, and the first extracellular loop (ECL1) undergo major conformational changes in secondary structure during peptide ligand binding, forming key interactions with the peptide. Hydrogen/deuterium exchange, disulfide cross-linking and molecular dynamics studies suggest that the stalk and ECL1 play critical roles in modulating peptide ligand binding and receptor activation. We further propose a dual-binding-site trigger model for GCGR activation, which requires conformational changes of the stalk, ECL1 and TMD. These insights into the full-length GCGR structure deepen our understanding about the signaling mechanisms of class B GPCRs.

Hongwei Wang –Tsinghua University

How small a protein can be solved at high resolution by single particle cryo-EM?

The fast development of single particle cryo-EM has made it more feasible to obtain the 3D structure of well-behaved macromolecules with molecular weight higher than 200 kDa at ~3Å resolution. On the other hand, it is a challenge to obtain high resolution structure of molecules smaller than 100 kDa using single particle cryo-EM, mainly due to the low contrast of the molecules embedded in vitreous ice. We have previously demonstrated that using a Cs-corrector-VPP coupled cryo-EM, near-atomic resolution can be obtained with both under- and over-focused micrographs. In this work, we applied the Cs-corrector-VPP coupled cryo-EM to study 52 kDa streptavidin (SA) protein absorbed on a thin layer of graphene film and embedded in vitreous ice. We were able to solve both the apo-SA and biotin-bound SA at near-atomic resolution using single particle cryo-EM. We found that the location of particle in the sample has a major impact on the quality of their fine details. Most of the particles contributing to the high resolution structure are on the graphene surface, while most of the particles absorbed to the air-water interface have lost their high-resolution structural information.

Ning Zheng –University of Washington

The inner workings of the COMPASS H3K4 methyltransferase complex

The SET1/MLL family of histone methyltransferases are conserved in eukaryotes and regulate transcription by catalyzing histone H3K4 mono-, di-, and tri-methylation. These enzymes form a common five-subunit catalytic core, whose assembly is critical for their basal and regulated enzymatic activities through unknown mechanisms. Here we present the crystal structure of the intact yeast COMPASS histone methyltransferase catalytic module, consisting of Swd1, Swd3, Bre2, Sdc1, and Set1. The complex is organized by Swd1, whose conserved C-terminal tail not only nucleates Swd3 and a Bre2-Sdc1 subcomplex, but also joins Set1 to construct a regulatory pocket next to the catalytic site. This inter-subunit pocket is targeted by a previously unrecognized enzyme-modulating motif in Swd3 and features a doorstop-style mechanism dictating substrate selectivity among SET1/MLL family members. By spatially mapping the functional components of COMPASS, our results provide a structural framework for understanding the multifaceted functions and regulation of the H3K4 methyltransferase family.

Concurrent Session 23: Protein and Organelle Homeostasis

Weixing Zong – Rutgers University
PI3 kinases in intracellular membrane trafficking
PI3Ks are lipid kinases central to numerous signaling pathways. Based on substrate specificity and sequence homology, PI3Ks are grouped into three classes: Class I, Class II, and Class III. Class IA PI3Ks are composed of a p85 regulatory subunit and a p110 catalytic subunit responsible for the production of PI(3,4,5)P3, which activates the AKT/mTOR signaling pathway. It is believed that Class IA PI3K inhibits autophagy by promoting nutrient uptake and metabolic activities through AKT/mTOR. In contrast, the Class III PI3K, Vps34, converts PI to PI(3)P, which is essential for autophagy initiation. Hence, the current dogma is that, in metazoans, Class III PI3K Vps34 activates autophagy while Class IA PI3Ks inhibits it. Using genetically modified mouse models, we study the molecular regulation and physiological significance of the Class I and Class III PI3 kinases in controlling intracellular membrane trafficking and protein homeostasis.

Quan Chen – Chinese Academy of Sciences
Molecular regulation of selective mitophagy and its role in inflammasome activation and hepatocarcinogenesis
Accumulating evidence has proved that mitochondrial metabolism and functions are closely linked with tumor initiation and progression. Mitophagy, a selective process that removes damaged or unwanted mitochondria, was suggested to play a role in mitochondrial quality control and metabolic reprogramming. Previously, we have revealed that FUNDC1, a mitochondrial outer-membrane protein, functions as a mitophagy receptor to mediate hypoxia-induced mitophagy. FUNDC1 harbors an LC-3 –interacting region (LIR) and interacts with LC-3 to mediate mitophagy both in cultured cell systems and in (patho-)physiological settings. Here we discover that enhanced expression of FUNDC1 protects against diethylnitrosamine (DEN)-induced HCC, whereas specific knockout of FUNDC1 in hepatocytes promotes HCC initiation and progression. Hepatocyte-specific FUNDC1 ablation results in the accumulation of damaged mitochondria and elicits a cascade of events involving inflammosome activation, leading to hyperproliferation of hepatocytes and promotion of hepatocellular carcinoma. Our results uncover the critical role of FUNDC1-mediated mitophagy in inflammasome activation and hepatocarcinogenesis.

Anbing Shi – Tongji Medical College, Huazhong University of Science and Technology
Worming Our Way Through the Endosomal System
RAB-10/Rab10 is a master regulator of endocytic recycling in epithelial cells. To better understand the regulation of RAB-10 activity we sought to identify RAB-10(GDP) interacting proteins. One novel RAB-10(GDP) binding partner that we identified, LET-413, is the C. elegans homolog of Scrib/Erbin. Here we focus on the mechanistic role of LET-413 in the regulation of RAB-10 within the C. elegans intestine. We show that LET-413 is a RAB-5 effector and colocalizes with RAB-10 on endosomes, and the overlap of LET-413 with RAB-10 is RAB-5-dependent. Notably, LET-413 enhances the interaction of DENN-4 with RAB-10(GDP) and promotes DENN-4 GEF activity toward RAB-10. Loss of LET-413 leads to cytosolic dispersion of RAB-10 effectors TBC-2 and CNT-1. Finally, we demonstrate that the loss of RAB-10 or LET-413 results in abnormal over-extensions of lateral membrane. Hence, our studies indicate that LET-413 is required for the DENN-4-mediated RAB-10 activation, and LET-413-assisted RAB-5 to RAB-10 cascade contributes to the integrity of C. elegans intestinal epithelia.

Qing Zhong –Shanghai Jiao Tong University School of Medicine
Biochemical Dissection and Reconstitution of Mammalian Autophagy
My lab focuses on the regulatory mechanisms of autophagosome biogenesis, substrate recruitments and autophagosome fusion with lysosomes. We have identified and characterized novel protein factors essential for autophagy initiation, cargo recruitment and

autophagosome-lysosome fusion, and developing effective measures in vivo and in vitro for these processes. We will report our recent work on biochemical reconstitution of the regulated fusion machinery that is required for autophagosome fusion with lysosomes.

Yonghao Yu –UT Southwestern Medical Center

Navigating downstream of mTORC1: A Quantitative Phosphoproteomic Approach

Phosphorylation is a critical mediator of insulin-stimulated signaling pathways. Indeed, many key players in the pathway, including insulin receptor, insulin receptor substrate, Akt and mTORC1, are either kinase themselves and/or phosphorylated upon insulin stimulation. A number of these phosphorylation events further modulate their corresponding biological activity, relaying the step-wise downstream signaling to coordinate many functions of insulin. The specific mechanisms of how aberrant regulation of this pathway contributes to the pathogenesis of diabetes, however, is still incompletely understood. We previously performed quantitative mass spectrometric analysis and identified hundreds of potential mTORC1 targets (Yu et al., Science, 2011). Detailed biochemical characterization of one such hit, Grb10, showed that it is a direct mTORC1 substrate. Grb10 is phosphorylated by mTORC1, which results in its stabilization and accumulation. Grb10 then functions as a pseudosubstrate that competitively inhibits the activity of insulin receptor and IGF1 receptor. Insulin-signaling pathways are known to differ in various cell types. Even though liver is one of the most important insulin-responsive organs, many aspects of insulin signaling in liver remains poorly understood, in part due to the lack of a suitable in vitro biological system. We recently performed quantitative phosphoproteomic analysis of insulin signaling in freshly isolated rat hepatocytes, which was shown to demonstrate robust responses to insulin in vitro. This system also allows the study of action of insulin without the influence from other hormonal and physiological changes that occur during the refeeding process in live animals. We characterized the phosphoproteome that is regulated by insulin, as well as its key downstream kinases including Akt, mTORC1 and S6K in rat hepatocytes. We identified a total of 10,670 unique, confidently localized phosphorylation sites on 3,440 proteins in this single cell type. Detailed bioinformatic analysis on each individual dataset identified both known and previously unrecognized targets of this key insulin downstream effector pathway. Furthermore, integrated analysis of the hepatic Akt/mTORC1/S6K signaling axis allowed the delineation of the substrate specificity of several close-related kinases within the insulin signaling pathway. We expect that the datasets will serve as an invaluable resource, providing the foundation for future hypothesis-driven research that helps delineate the molecular mechanisms that underlie the pathogenesis of type 2 diabetes and related metabolic syndrome.

Liangyi Chen – Peking University

Fast, long-term super-resolution imaging with Hessian structured illumination microscopy and its application in clinical samples

To increase the temporal resolution and maximal imaging time of super-resolution (SR) microscopy, we have developed a deconvolution algorithm for structured illumination microscopy based on Hessian matrixes (Hessian-SIM). It uses the continuity of biological structures in multiple dimensions as a priori knowledge to guide image reconstruction and attains artifact-minimized SR images with less than 10% of the photon dose used by conventional SIM while substantially outperforming current algorithms at low signal intensities. Hessian-SIM enables rapid imaging of moving vesicles or loops in the endoplasmic reticulum without motion artifacts and with a spatiotemporal resolution of 88 nm and 188 Hz. Its high sensitivity allows the use of sub-millisecond excitation pulses followed by dark recovery times to reduce photobleaching of fluorescent proteins, enabling hour-long time-lapse SR imaging of actin filaments in live cells. We observed the structural dynamics of mitochondrial cristae and structures that, to our knowledge, have not been observed previously, such as enlarged fusion pores during vesicle exocytosis. Finally, we demonstrate the robustness of the system in imaging fibroblasts and iPS cells derived from human, which readily differentiates difference in mitochondrial structures between normal people and

patients.

Concurrent Session 24: Development and Human Diseases

Xin Sun – University of California, San Diego
Consider the Lung as a Sensory Organ
At resting, an average person inhales/exhales 5-8 litters of air. This air may vary in oxygen content, carry allergen, pollutants or pathogens. To address how the lung senses and responds to these signals, we focused on pulmonary neuroendocrine cells (PNECs). PNECs are rare airway epithelial cells that are preferentially localized to airway branch point junctions. They are innervated by nerves, and can produce potent neuropeptides, neurotransmitters and amines. Our data suggest that proper aggregation of PNECs into neuroepithelial bodies is essential for their normal function. Disruption of PNEC clustering led to increased PNEC products and heightened baseline immune signature. We are currently testing the hypothesis that these cells serve as key nodes that mediate lung, environment, immune and nervous system interactions.

Yi Arial Zeng – Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, Shanghai
Protein C Receptor In Regulating Mammary Stem Cells And Breast Cancer
The mammary gland is composed of multiple types of epithelial cells that are generated by mammary stem cells (MaSCs) residing at the top of the hierarchy. The identity of MaSCs was unclear. Our study demonstrates that Procr (Protein C receptor), a novel Wnt-target in the mammary gland, marks a population of multipotent MaSC. Procr-expressing cells display high regenerative capacity in transplantation assays and differentiate into all lineages of the mammary epithelium by lineage tracing. In mouse, Procr was required for the mammary development and homeostasis, and was important for the initiation of mammary tumor. Triple-negative breast cancer (TNBC) is a highly aggressive malignancy with no targeted treatment option. We found that PROCR is highly expressed in TNBC patient samples, and associated with poor prognosis. Remarkably, targeting PROCR by a neutralizing antibody inhibits TNBC tumor growth. PROCR represents a surface therapeutic target for human TNBC.

Ting Chen – National Institute of Biological Sciences, Beijing
Mesenchymal niche heterogeneity and plasticity governs regional epithelial tissue regeneration and disease initiation
Niche cells play dominant roles in instructing the activity of stem cells (SCs) and progenitor cells. However the principles governing organ level niche cells heterogeneity and functional diversity are largely unknown. Here we discover that the mesenchymal niche cells can be reprogrammed to change the regeneration landscape of epithelial SCs. Our transcriptome screen revealed that the expression of Hoxc genes in adult skin dermis uniquely correlates with the regional regeneration pattern of hair follicles (HFs). Disrupting the region specific expression pattern of Hoxc genes by either decreasing epigenetic repression through loss of Bmi1, or ectopic interaction of the Hoxc locus with an active epigenetic region, leads to ectopic HF regeneration. In vivo single Hoxc gene is sufficient to convert dormant dermal papilla (DP) niche into active one capable of driving regional HF regeneration through canonical Wnt signaling. Our results reveal that Hoxc genes bestow organ level mesenchymal niche heterogeneity and plasticity.

Ji-Feng Fei – Institute of Brain Research and Rehabilitation, South China Normal University
Axolotl, an ideal model for dissecting the mystery of spinal cord regeneration
Human spinal injury causes permanent disabilities due to the poor regenerative capability in humans and the lack of effective clinical therapies. Unlike mammals, salamanders can fully regenerate their spinal cords upon transection or tail amputation. This makes salamander a powerful model for dissecting the underlying molecular mechanisms of spinal cord regeneration. In order to create a deeper understanding of the molecular mechanisms during axolotl spinal cord development and regeneration, we have sequenced and assembled the

entire axolotl (Ambystoma Mexicanum, a type of salamanders) genome (around 32Gb), the largest genome assembled so far. Moreover, we have applied CRISPR/Cas9 techniques and achieved efficient knockout of targeted genes, as well as knock-in of exogenous sequences into defined axolotl genomic loci. Making use of the advantages of established techniques, we have demonstrated the essential role of Sox2 during spinal cord regeneration. We were also able to faithfully label neural stem cells, which have been difficult to label genetically via classical transgenesis, via insertion of a reporter gene into the axolotl Sox2 genomic locus. Our work has opened up opportunities to thoroughly investigate the mechanisms of axolotl spinal cord development and regeneration, that may shed light on creating new therapies in humans.

Pengyu Huang – School of Life Science and Technology, Shanghai Tech University, Shanghai

Regulation of liver regeneration during chronic liver injuries

Liver regeneration happens after various types of injuries. Unlike the well-studied liver regeneration caused by partial hepatectomy, there is accumulating evidence suggesting that liver regeneration during other injuries may result from some unknown mechanism. We have systematically analyzed liver samples from acute and chronic liver injury mice. we found that insulin-like growth factor 2 (IGF-2) was drastically induced following the liver injuries caused by tyrosinemia or long-term treatments of carbon tetrachloride (CCl_4). However, it was not observed during the early phase of acute liver injuries after partial hepatectomy or single treatment of CCl_4. Remarkably, most of IGF-2 expressing hepatocytes were located at the histological area around the central vein of liver lobule after the liver injuries caused either in Fah-deficient mice or in CCl_4 chronically treated mice. Hepatocyte proliferation in vivo was significantly promoted by the induced IGF-2 over-expression, which could be inhibited by AAV-delivered IGF-2 shRNAs or linsitinib, an inhibitor of IGF-2 signaling. Proliferating hepatocytes in vivo responded to IGF-2 via both insulin receptor and IGF-1 receptor. IGF-2 also significantly promoted DNA synthesis of primary hepatocytes in vitro. More interestingly, the significantly induced IGF-2 was also found to co-localize with glutamine synthetase in the region enriched with proliferating hepatocytes for the liver samples from patients with liver fibrosis. When we analyzed human liver fibrosis samples, we also noticed that some hepatocytes underwent regulated non-apoptotic cell death, which could also be found in one liver injury mouse model. Based on this mouse model, we also identified several genes that protected hepatocytes from death.

Dali Li – East China Normal University

Genome editing for diseases modeling and gene therapy

There are more than 7,000 rare diseases among which 80% of the diseases are caused by genetic mutations. To date, approximately 95% of genetic disorders have no approved treatments. Gene therapy is a promising strategy for certain of hereditary diseases and great progresses have been made in recent years, but current strategies have some disadvantages, such as short duration of exogenous gene expression or tumorigenic potential. To test the feasibility of gene therapy for specific disease, genetically modified animal models are valuable tools to evaluate the curative effects of the treatments. However, ES cell based gene targeting is time and labor consuming process which limits the scale of generation of mutant animal models. In addition, this technology is not applicable in other model organisms whose ES cell lines are not established or difficult for handling in many laboratories. Taking the advantage of Cas9/sgRNA induced site-specific double strand DNA break which efficiently stimulates homologous recombination with the presence of donor DNA, we generated site-specific knockin strains to mimic human genetic disorders. Using liver as the target organ, through injection of Cas9/Cas9n together with donor templates, we successfully cure certain inheritable diseases, such as hemophilia and hereditary tyrosinemia via site-specific correction of causer mutations. Moreover, we also established a method to enhance recombinant adeno-associated virus infection, which significantly improves genome editing efficiency and gene therapy efficacy. The engineered nucleases

are revolutionary technologies for production of disease models as well as promising strategies for genetic disorder therapeutics.

Yan Song – School of Life Sciences, Peking-Tsinghua Joint Center for Life Sciences, Peking University

Commitment matters: Timely and robust cell fate commitment in neural stem cell lineages

Asymmetric stem cell division establishes an initial difference between a stem cell and its differentiating sibling, critical for maintaining homeostasis and preventing carcinogenesis. However, the mechanisms that consolidate and lock in such initial fate bias remain obscure. By performing in vivo time-lapse live imaging of neural stem cells (NSCs) in the Drosophila central brain, we unexpectedly revealed the existence of a tightly-regulated yet previously-overlooked transition phase between the initial cell fate decision and the ultimate cell fate commitment. We identified the super elongation complex (SEC), best known for transcription elongation checkpoint control, as an intrinsic amplifier that accelerates this transition stage and thereby drives NSC fate commitment. Mechanistically, SEC is highly expressed in NSCs, where it promotes self-renewal by physically associating with Notch transcription activation complex and enhancing HES gene transcription. HES in turn upregulates SEC activity, forming a self- reinforcing feedback loop with SEC. SEC inactivation leads to NSC loss, whereas its overactivation results in neural progenitor dedifferentiation and tumorigenesis. Our studies therefore unveiled an SEC- mediated intrinsic amplifier mechanism in ensuring timeliness and robustness in NSC fate commitment. In addition, our latest unpublished work revealed a safeguard mechanism whereby a protein trafficking regulatory complex acts as bomb squad to recognize and retrieve potentially harmful Notch receptors and transport them away in a timely manner to ensure neural progenitor fate commitment and prevent progenitor-derived tumorigenesis. Together, our studies deciphered key principles underlying timely and robust cell fate commitment and provided new mechanistic explanations for carcinogenesis.

Bo Zhou – Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences

When hematopoietic stem cells meet puberty

Hematopoietic stem cells (HSCs) are tightly regulated at different developmental stages regarding their number and self-renewal capacity. Many pathways have been implicated in regulating HSC development in cell-autonomous manners. However, it remains unclear how HSCs sense and integrate developmental cues into their properties. In this study, we identified an extrinsic mechanism by which HSC number and functions are regulated during mouse puberty. We found that the HSC number in postnatal bone marrow reached homeostasis at 4 weeks after birth. Luteinizing hormone (LH), but not downstream sex hormones, was involved in regulating HSC homeostasis during this period. LH receptor (Lhcgr) highly restricted its expression in HSCs and multipotent progenitor cells in the hematopoietic hierarchy. When Lhcgr was deleted, HSCs continued to expand even after 4 weeks after birth, leading to abnormally elevated hematopoiesis and leukocytosis. In a murine acute myeloid leukemia model, leukemia development was significantly accelerated upon Lhcgr deletion. Together, our work revealed an extrinsic counting mechanism that restricts HSC expansion during development, which is physiologically important for maintaining normal hematopoiesis and inhibiting leukemogenesis.

Concurrent Session 25: Liver Physiology and Metabolic Homeostasis

Xiao-bo Zhong, University of Connecticut
Control of postnatal liver maturation by nuclear receptors and lncRNAs
The liver is a vital organ with critical functions in metabolism of various biological materials, synthesis of several vital proteins, detoxification of toxic substances, and immune defense. Most liver functions are not mature at birth and many changes happen during postnatal liver development, which lead to differential vulnerabilities of the liver at different developmental stages. However, the details of what changes occur in liver after birth, at what developmental stages they occur, and molecular mechanisms in the regulation of the developmental process are not clearly known. We used mouse as an animal model to monitor transcriptome signatures of mRNAs by RNA-Seq and defined a clear timeline of functional transition from prenatal through neonatal and adolescent to adult in C57BL/6 mice. Same approach was applied to nuclear receptor farnesoid X receptor knockout *Fxr*$^{-/-}$ mice and found that activation of neonatal-specific pathways was prolonged and maturation of multiple metabolic pathways was delayed without FXR. The RNA-Seq data were further used to define ontogenic expression patterns of long non-coding RNAs (lncRNAs) during liver maturation. Similarly to coding mRNAs, lncRNAs also displayed three major ontogenic patterns associated with functional transition. Neighboring coding and non-coding RNAs showed the trend to exhibit highly correlated ontogenic expression patterns. Functions of transcription factor, hepatocyte nuclear factor 1 alpha (HNF1a) and its neighboring lncRNA, HNF1a-AS1, were further determined with a siRNA knockdown approach in human liver HepaRG and Huh7 cells. The study demonstrated a critical role of HNF1a-AS1 in the regulation of expression and function of detoxification P450 enzymes.

Wen Xie, University of Pittsburgh
Disease effect on liver metabolism
Drug metabolism and disposition are critical in maintaining the chemical and functional homeostasis of xenobiotics and endobiotics. Accumulating evidence suggests that many hepatic and systemic diseases can affect drug metabolism and disposition in the liver by regulating the expression and/or activity of drug-metabolizing enzymes and transporters in the liver. This presentation will focus on our recent study showing how chronic inflammatory liver diseases affect the metabolism of estrogens in the liver through the transcriptional regulation of sulfonation and de-sulfonation pathways. Understanding the disease effect on drug metabolism has great implications in personalized medicine.

Chaohui Yu, Zhejiang University
Vitamin D receptor (VDR) and non-alcoholic fatty liver disease (NAFLD)
Nonalcoholic fatty liver disease (NAFLD) is the hepatic manifestation of the metabolic syndrome. Various nuclear receptors are involved in the pathogenesis of NAFLD. Vitamin D receptor (VDR) is an important nuclear receptor that regulates expression of variety of genes relating to cell proliferation, differentiation, apoptosis, and immune regulation. Relationship of plasma vitamin D levels and development of NAFLD has been reported in a number of studies during recent years. Whether VDR takes part in NAFLD and its specific mechanism is not clear. Recently, we found that high fat diet induced increased hepatic VDR expression in mice. Hepatic-specific knockout of VDR aggravated high fat diet-induced hepatic steatosis and insulin resistance. Mechanistically, VDR regulated hepatic steatosis, inflammation, and insulin sensitivity through NF-κB signaling and IRS1-AKT signaling. Our results suggest a significant role of VDR in the progression of NAFLD and provide a potential therapeutic target for NAFLD.

Wendong Huang, Beckman Research Institute of City of Hope
Bile acid receptors in regulating fatty liver diseases
Bile acids (BAs) are primarily known for their roles as liver-produced and secreted molecules that aid in the emulsification and absorption of lipids in the small intestine. Recent studies

from my group and others indicate that BAs also act as hormones that can alter metabolism through targeting the nuclear farnesoid X receptor (FXR, NR1H4) and the cell membrane-associated G protein-coupled BA receptor 1 (GPBAR-1, MBAR1, hereafter referred to as TGR5). Bariatric surgery is an effective clinical intervention given its ability to achieve greater and more sustainable weight loss as well as improvement of fatty liver diseases. To date, Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) represent the two most commonly performed bariatric surgeries; both surgical interventions induce significant weight loss and improve metabolism in humans and rodent models. Our results indicate that VSG strongly alters the bile acid profile. Fxr knockout mice almost completely lose the VSG's beneficial effects. In addition, TGR5 is required to maintain the effects of anti-obesity, anti-hyperglycemia, and fatty liver improvements of VSG in mice. VSG results in an enhancement of TGR5 signaling, concomitant with improved metabolism and increased energy expenditure. Moreover, we have also investigated the genome-wide transcriptome and regulatory changes after VSG in mouse liver by RNA-Seq and FAIRE-Seq. The results showed that VSG upregulated the expression of CYP450 genes participating in linoleic acid metabolism. Furthermore, lipidomics study confirmed the changes of lipid metabolism by VSG. Therefore, VSG may reverse the high fat-induced dysregulation of lipid metabolism in the liver and other organs.

Shi-mei Zhuang, Sun Yat-Sen University

Vessels that encapsulate tumor clusters (VETC) in HCC metastasis and therapeutic response

Although thousands of long noncoding RNAs (lncRNAs) have been annotated, only a limited number of them have been functionally characterized. Here we identified a novel oncogenic lncRNA (named lnc-UCID) that is frequently amplified and upregulated in hepatocellular carcinoma (HCC), and higher lnc-UCID level was correlated with shorter recurrence-free survival of HCC patients. Both gain- and loss-of function studies revealed that lnc-UCID could promote G1/S transition and cell proliferation, and silencing lnc-UCID expression significantly inhibited hepatoma cell growth *in vitro* and *in vivo*. Mechanistically, lnc-UCID enhanced CDK6 expression by competitively binding to DHX9 and sequestering DHX9 from CDK6-3'UTR. These findings provide new insights into the biological functions of lncRNAs in HCC development and highlights lnc-UCID as a potential target for anti-cancer therapy.

Ai-ming Yu, University of California at Davis

ncRNAs in the control of liver metabolism and hepatocellular carcinoma (HCC)

Liver is the major organ for the catabolism/metabolism of proteins, hormones, and many other essential biochemicals as well as xenobiotics that are governed by large cassettes of hepatic enzymes and transporters. Noncoding RNAs (ncRNAs) such as microRNAs (miRs or miRNAs) transcribed from human genome have been recognized as critical factors in the control of hepatocyte functions via the regulation of target gene expression including hepatic enzymes and transporters. Indeed liver cancer especially the most prevalent hepatocellular carcinoma (HCC) exhibit dysfunction in cell metabolism (e.g., glucose and amino acid metabolism) and dysregulation of solute carrier (SLC) transporters and metabolic enzymes. Therefore, targeting of liver metabolism via ncRNA pathways represents a new strategy for management of HCC. This talk will present some recent findings on miRNA-controlled regulation of SLC transporters and subsequent impact on HCC cell metabolism. In addition, I will present new results on the application of bioengineered miRNA agents (BERAs) as possible therapeutics for the treatment of HCC in orthotropic xenograft tumor mouse models. These findings suggest that restoration of endogenous miRNA expression or function depleted in cancer cells holds promise in modulating cancer cell metabolism and treating lethal HCC.

Huichang Bi, Sun Yat-Sen University

Pregnane X receptor in hepatomegaly and liver regeneration

Activation of pregnane X receptor (PXR), a nuclear receptor that controls xenobiotic and

endobiotic metabolism, is critical in regulating drug disposition and is known to increases liver size and causes liver hypertrophy. However, only a few studies have explored the role of PXR in liver regeneration, and the exact mechanism, by which PXR induces liver growth, especially how PXR interacts with the cellular proliferation machinery, remains unclear. In this study, the effect of PXR activation on liver enlargement and cell change was evaluated in several strains of genetically-modified mice and animal models. Lineage labelling using AAV-*Tbg*-Cre-treated *Rosa26*^{EYFP} mice or *Sox9-Cre*^{ERT}, *Rosa26*^{EYFP} mice was performed and *Pxr*-null mice or AAV *Yap* shRNA-treated mice were used to confirm the role of PXR or YAP. Treatment with selective PXR activators induced liver enlargement and accelerated regeneration in wild-type and *PXR*-humanized mice but not in *Pxr*-null mice by increase of cell size, induction of a regenerative hybrid hepatocyte (HybHP) reprogramming, and promotion of hepatocyte and HybHP proliferation. Mechanistically, PXR interacted with yes-associated protein (YAP) and PXR activation induced nuclear translocation of YAP. Blockade of YAP abolished PXR-induced liver enlargement in mice. These findings revealed a novel function of PXR in enlarging liver size and changing liver cell fate via activation of the YAP signalling pathway. These results have implications for understanding the physiological functions of PXR and suggest the potential for manipulation of liver size and liver regeneration.

Hua Wang – First Affiliated Hospital, Institute for Liver Diseases of Anhui Medical University, Hefei, Anhui, China

PPAR and liver regeneration

Peroxisome proliferator-activated receptor □ (PPAR□) is a key nuclear receptor involved in the control of lipid homeostasis. In rodents, PPAR□ is also a potent hepatic mitogen. Hepatocyte-specific disruption of PPAR□ inhibits agonist-induced hepatocyte proliferation, little is known about the role of PPAR□ in partial hepatectomy (PHx)-induced liver regeneration. Here, using hepatocyte-specific PPAR□ deficient (*Ppara*$^{\Delta Hep}$) mice, the function of hepatocyte PPAR□ in PHx-induced liver regeneration was investigated. PPAR□ expression was significantly increased in the liver after PHx. Comparing with the wild-type mice, *Ppara*$^{\Delta Hep}$ mice exhibited significantly reduced hepatocyte proliferation at 32 hours after PHx. Consistently, reduced *Ccnd1* and *Pcna* mRNA and CYCD1 and PCNA protein were observed at 32 hours after PHx in *Ppara*$^{\Delta Hep}$ mice. Furthermore, *Ppara*$^{\Delta Hep}$ mice showed increased hepatic lipid accumulation and enhanced hepatic triglyceride contents due to impaired hepatic fatty acid β-oxidation when compared with that in wild-type *Ppara*$^{fl/fl}$ mice. These results suggest that PPAR□ promotes liver regeneration after PHx at least partially via regulating the cell cycle and lipid metabolism.

Concurrent Session 26: Systems Biology and Omics

Sheng Zhong – University of California, San Diego,
Rainbow-seq: combining cell lineage tracing with single-cell RNA sequencing in preimplantation embryos
We developed the Rainbow-seq technology to trace cell division history and reveal single-cell transcriptomes. With distinct fluorescent protein genes as lineage markers, Rainbow-seq enables each single-cell RNA-seq experiment to simultaneously decode the lineage marker genes and read single-cell transcriptomes. We triggered lineage tracking in each blastomere at 2-cell stage, observed microscopically inequivalent contributions of the progeny to the two embryonic poles at the blastocyst stage, and analyzed every single cell at either 4- or 8-cell stage with deep paired-end sequencing of full-length transcripts. Although lineage difference was not marked unequivocally at a single-gene level, the lineage difference became clear when the transcriptome was analyzed as a whole. Moreover, several groups of novel transcript isoforms with embedded repeat sequences exhibited lineage difference, suggesting a possible link between DNA demethylation and cell fate decision. Rainbow-seq bridged a critical gap between division history and single-cell RNA-seq assays.

Xiu-Jie Wang – Institute of Genetics and Developmental Biology
m^{6}A RNA modification: mechanism, function and social implications
As the most abundant modification on mRNAs, N6-methyladenosine (m6A) has been recently identified as an important regulator for many essential biological processes. m6A modification usually occurs on adenosine within RRACH motifs, but usually only a small proportion of adenosine within the RRACH motif are methylated at certain cell stage. We have identified that the selectivity of m6A modification sites are regulated by miRNAs via sequencing pairing, revealing a novel function of miRNAs in regulating mRNA epigenetic modification. We also systematically characterized the function of m6A modification in regulating mouse cerebellum development and functions. Intriguingly, we found that the formation of m6A modification can enhance the efficacy of hippocampus-dependent memory consolidation by regulating early-response genes, yet excessive training can somehow compensate the function of m6A in regulating long term memory formation.

Bin Zhang – Icahn School of Medicine at Mount Sinai
Network Modeling of Large-scale Multi-Omics Data Reveals Novel Pathways and Key Regulators in Alzheimer's Disease
Alzheimer's disease (AD) is the most common form of degenerative dementia. Genetic, pathological, neuroimaging data reveal that AD involves many different pathways across many different brain tissues. Rare mutations in APP, PSEN1 and PSEN2 have been identified in early-onset familial AD and about two dozens of genetic loci have been associated with the more common late-onset Alzheimer´s disease. However, the molecular basis of AD development and progression remains elusive. Increasingly available large scale genetic, genomic, proteomic and pathophysiological data in AD have made it possible to more comprehensively address the complex mechanisms and effectors of AD through application of advanced systems biology approaches. We have developed a multiscale network modeling framework to integrate multi-Omics data in AD. Towards this end, we constructed gene regulatory networks from thousands of postmortem brain tissue samples across many brain regions from AD and normal control subjects. Thousands of gene subnetworks were identified and systematically examined with respect to known pathways, AD related gene sets, and AD clinical and pathophysiological data. These subnetworks were rank-ordered by the degree of dysregulation and relevance to AD pathology. The network drivers were systematically identified based on network connectivity. Network structures of a number of top ranked subnetworks were systematically validated through in vitro or in vivo perturbations of key network driver genes. Our integrative multiscale network analysis identified novel pathways and drivers that potentially regulate AD pathogenesis.

Yong Zhang, School of Life Science and Technology, Tongji University
Inherited epigenetic signatures prime the establishment of zygotic transcriptional regulation during early embryogenesis
For animals, epigenetic modifications can be globally or partially inherited from gametes after fertilization, and such information is required for proper zygotic transcriptional regulation, especially during the process of zygotic genome activation. However, the mechanism underlying how the inherited epigenetic signatures affect transcriptional regulation during early embryogenesis remains poorly understood. We built a probabilistic model of DNA methylation level changes along the process of cell division, and applied that model to two issues related with the establishment of zygotic transcriptional regulation. In the first part of this talk, I will discuss the contribution of inherited H3K9me3 asymmetry on DNA methylation-dependent imprinting in mouse pre-implantation embryos. The application of the probabilistic model showed that H3K9me3 signals in gametes generally contribute to the escape of DNA de-methylation in mouse pre-implantation embryos. We further found the inherited H3K9me3 asymmetry can specify DNA methylation-dependent imprinting, and novel ICRs can be identified based on the synergistic asymmetry of H3K9me3 and DNA methylation. In the second part of this talk, I will discuss the programmed epigenetic heterogeneity before asymmetric cell division in human pre-implantation embryos. The probabilistic model can largely predict the DNA methylation heterogeneity among cells within the same embryo during human early embryogenesis, and such programmed DNA methylation heterogeneity may play a role in the first cell-fate determination.

Li Yang, CAS-MPG Partner Institute for Computational Biology
Harness unintended nucleic acid mutation to targeted base editing
Members of APOBEC/AID (the apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like or activation-induced cytidine deaminase) family catalyze cytidine-to-uridine (C-to-U) base substitutions in RNA, viral DNA and genomic DNA. The APOBEC-induced cytidine deamination in single-stranded DNA (ssDNA) in the genomic region around single-strand break (SSB) or DNA double-strand break (DSB) leads to unintended mutations. Interestingly, single stranded nucleic acids are prevalent in CRISPR–Cas9-mediated gene editing processes. We show that nCas9-generated paired SSBs can be processed by DNA exonucleases (such as MRE11) to form ssDNAs. APOBEC/AID proteins recognize these genomic ssDNAs and trigger C-to-U deamination, which can be further processed to yield unwanted mutations, including point mutations and insertions/deletions (indels). As expected, temporarily suppressing endogenous APOBECs represses these unwanted mutations1. In addition to these unwanted mutations, targeted C-to-T base editing are achieved by combining rat APOBEC1 with CRISPR/Cas9, referred to as base editor (BE) system. Mechanically, Cas9- /Cas9 variant- fused APOBEC/AID can be guided to target site by sgRNA to introduce programmed C-to-T substitution at the single-base level. The frequency of C-to-T base editing is further improved by inhibiting unwanted mutations with conjugated UGI in BE. Finally, a series of novel BEs are recently developed by linking catalytically dead Cpf1 with rat APOBEC1 (dCpf1-BE), or by linking Cas9 nickase with human APOBEC3A (hA3A -BE). Given that Cpf1 requires a T-rich PAM sequence for target-DNA recognition and that hA3A can catalyze efficient deamination of methylated cytidines, these newly-constructed BEs achieves targeted C-to-T base editing in expanded genomic regions/backgrounds with high precision.

Kun Zhang – University of California, San Diego
Integrative single-cell analysis by transcriptional and chromatin states of the brain
Detailed characterization of the cell types comprising the highly complex mammalian brain is essential to understanding function. Such tasks require highly scalable experimental approaches to examine different aspects of the molecular state of individual cells, as well as the computational integration to produce unified cell state annotations. To this end, we have developed methods to acquire nuclear transcriptome and DNA accessibility maps in tens of thousands of single cells from the mouse and human brain. This has led to the best-resolved

human neuronal subtypes to date, identification of a majority of the non-neuronal cell types, as well as the cell-type specific nuclear transcriptome and DNA accessibility maps. Integrative chromatin/transcriptome analysis allowed us to identify transcription factors and regulatory elements shaping the state of different brain cell types, and to map genetic risk factors of human brain common diseases to specific pathogenic cell types and subtypes.

Concurrent Session 27: New Investigators Session II

Liang Chen – Wuhan University
R-loop: A Unique Nucleic Acid Structure in Relation to Transcription Regulation and Disease
R-loop is a three stranded structure formed upstream of an elongating RNA polymerase. It is composed of a newly synthesized nascent RNA that anneals back to the template DNA strand, and the displaced non-template DNA strand. Increasing evidence suggests both physiological and pathological effects of R-loops in cells. On one hand, R-loops are actively involved in the regulation of transcription, epigenetic dynamics and replication; on the other hand, persistent R-loops often result in genome instability, which is associated with many diseases, such as cancers and neurodegenerative diseases. In order to gain more insight into the R-loop dynamics in relation to transcription regulation, we developed a new method, called R-ChIP, for genome-wide mapping of R-loops in vivo. By R-ChIP, we have identified unique sequence features and epigenetic configurations that are prone to R-loop formation, and showed a close tempo-spatial relationship between R-loop level and RNAPII activity on chromatin, all of which constitute molecular bases for the control of R-loop dynamics. We further applied R-ChIP to the study of myelodysplastic syndrome with splicing factor mutations in blood cells and identified a universal yet splicing independent disease mechanism. Specifically, disease-causing mutations in major splicing factors interfere with transcription, leading to augmented R-loops and replication stress. Such molecular defects ultimately result in increased DNA damage response and compromised proliferation of bone marrow-derived blood progenitors. In sum, our studies reveal that R-loop is a highly dynamic nucleic acid structure that links basic transcription regulation to disease development.

Pu Gao – Institute of Biophysics
Host-Pathogen Interaction: Pathogen-Mediated Non-Canonical Ubiquitination
Ubiquitination constitutes one of the most important signaling mechanisms in eukaryotes. Conventional ubiquitination is catalyzed by the universally conserved E1-E2-E3 three-enzyme cascade in an ATP-dependent manner. The newly identified SidE family effectors of the pathogen *Legionella pneumophila* ubiquitinate several human proteins by a novel mechanism without engaging any of the conventional ubiquitination machinery. We now report the crystal structures of SidE alone and in complex with ubiquitin, NAD, and ADP-ribose, thereby capturing different conformations of SidE before and after ubiquitin and ligand binding. The structures of ubiquitin bound to both mART and PDE domains reveal several unique features of the two reaction steps catalyzed by SidE. Further, the structural and biochemical results demonstrate that SidE family members do not recognize specific structural folds of the substrate proteins. Our studies provide both structural explanations for the functional observations and new insights into the molecular mechanisms of this non-canonical ubiquitination machinery

Jiazhi Hu – Peking University
Studying genome stability during genome editing by primer-extension sequencing
Efficient and precise genome editing is crucial for clinical applications and generating animal models, which requires engineered nucleases with high editing ability while low off-target activity. Here we present a high-throughput sequencing method, primer-extension-mediated sequencing (PEM-seq), to comprehensively assess both editing ability and specificity of engineered nucleases. We showed CRISPR/Cas9-generated breaks could lead to chromosomal translocations and large deletions by PEM-seq. Using PEM-seq, we also found xCas9 exhibited lower editing efficiency at certain loci, despite broader range of protospacer adjacent sequences and higher specificity compared to wild-type SpCas9. Moreover, we found AcrIIA4 inhibitor could greatly reduce the activities of SpCas9, whereas off-target loci were not so effectively suppressed as the on-target sites. We developed a new high-fidelity Cas9 variant that could significantly reduce the off-target activity during gene editing, which was validated by PEM-seq. These results suggest that PEM-seq is of great

use for optimizing genome editing strategy.

Sheng Wang – Shanghai Institute of Biochemistry and Cell Biology
Structure-Based Ligand Discovery Against Dopamine Receptor
Dopamine receptors are implicated in the pathogenesis and treatment of nearly every neuropsychiatric disorder. Although thousands of drugs interact with these receptors, our molecular understanding of dopaminergic drug selectivity and design remains clouded. To illuminate dopamine receptor structure, function, and ligand recognition, we determined crystal structures of the D4 dopamine receptor in its inactive state bound to the antipsychotic drug nemonapride, with resolutions up to 1.95 angstroms. These unusually high-resolution structures enabled a structure-based campaign for new agonists of the D4 dopamine receptor.
Here, we investigate docking screens of over 170 million make-on-demand, lead-like compounds. 549 molecules were synthesized and tested from among top docking ranks, and also from intermediate and low ranks. On testing, hit rates fell monotonically with score, ranging from 24% for the highest ranking, declining through intermediate scores, and dropping to a 0% hit rate for the lower ranks. Integrating across the resulting hit-rate curve predicts 453,000 D4 dopamine receptor active molecules in 72,600 scaffolds. Of the 81 new D4 dopamine receptor actives found here, 30 had Ki values < 1 μM. The most potent was a 180 pM Gi-biased, subtype-selective, full agonist, among the most potent subtype selective agonists known for D4.
The ability to efficiently exploit structure for specific probe discovery—rapidly moving from elucidating receptor structure to discovering previously unrecognized, selective agonists—testifies to the power of structure-based approaches.

Hui Yang – Institute of Biochemistry and Cell Biology
Recognition mechanism and inhibition of DNA targeting by CRISPR-Cas systems
The CRSIPR-Cas systems were found in almost all archaea and about 50% of bacteria and function as RNA-guided adaptive defense systems. The CRISPR-Cas systems can be grouped into two classes and subdivided into 6 types and 19 subtypes: Class 1 systems rely on multi-subunit surveillance ribonucleoprotein complexes termed Cascade, while Class 2 systems rely on single Cas protein involved ribonucleoprotein complexes. In turn, phages have developed divergent strategies to overcome CRISPR-Cas systems in host via a series of anti-CRISPR proteins through repressing the activity of effector proteins, which provide opportunities to act as 'off-switches' tools. To date, CRISPR-Cas systems are successfully applied to genome edit in both eukaryote and prokaryote. Further knowledge is required to minimize side effects resulting from alternate cleavage patterns, thereby insuring effective and safe genome editing in the clinic. The understanding of cleavage and inhibition mechanisms provide clues for goals to improve fidelity and efficiency, reduce off-target rate, and spatially and temporarily control activity of CRISPR-Cas systems. We focus on precise recognition and cleavage mechanisms of effector complexes in CRISPR-Cas systems, as well as the inhibition and regulation of these effector complexes. Our findings provide clues and structural information for related applications of these CRISPR-Cas systems.

Di Zhao – The University of Texas MD Anderson Cancer Center
Synthetic essentiality of chromatin remodeling factor CHD1 in PTEN deficient cancer
Prostate cancer (PCa) is one of the most common cancer types in mem. Advanced PCa, especially metastatic castration resistant prostate cancer (mCRPC), has high morbidity and mortality. ~50% advanced PCa shows PTEN deletion or mutation, therefore, identification of specific therapeutic targets for PCa harboring PTEN deficiency holds hope for patients with advanced PCa. Taking advantage of the vast public available prostate cancer genome database, we recently explored a novel approach to identify potential therapeutic targets by screening for "synthetic essential" genes that were occasionally deleted in cancer but always retained in the context of tumor suppressor gene deficiency. Using this method, we identified the chromodomain-helicase-DNA-binding protein 1 (CHD1) as a synthetic essential gene in

PTEN-deficient PCa. Both human PCa xenograft models and genetically engineered PCa mouse models suggested that depletion of CHD1 suppresses the tumor growth and progression of PTEN-deficient PCa, but has minimal effects on normal prostate tissue or PTEN-intact PCa. Importantly, CHD1 inhibition leads to a significantly prolonged overall survival in PTEN-loss PCa mouse model. Mechanistically, we found that PTEN-PI3K-AKT-GSK3β pathway regulates CHD1 phosphorylation, followed by ubiquitination and degradation via β-TrCP mediated proteasome pathway. The ChIP-seq and transcriptional profiling analyses uncovered that, in PCa with PTEN loss, CHD1 is stabilized and interacts with epigenetic marker H3K4me3, resulting in the transcriptional activation of NF-κB network genes. Furthermore, immunophenotyping using Mass Cytometry (CyTOF) and functional validation suggested that CHD1 contributes to the immunosuppressive tumor microenvironment in PCa through stimulating the expansion and activation of myeloid-derived suppressor cell (MDSCs) and reducing tumor-infiltrating CD8+ T-cells. Together, this study demonstrated that CHD1 plays important roles in tumor initiation and progression of PTEN-deficient PCa, and presents a promising context-specific therapeutic target in PCa. In addition, the novel approach of “synthetic essentiality” we proposed provides a good tool to identify context-specific therapeutic targets for undruggable tumor suppressor deficiency in cancer genome.

Concurrent Session 28: Abstract Session II (Cancer biology)

Jingwu Xie – Indiana University School of Medicine
Drug resistance in gastric and pancreatic cancer
Drug resistance is a major hurdle in management of cancer, and understanding drug resistance at the molecular levels may pave a way for effective treatment of cancer. Drug resistance can be intrinsic or adaptive. We used drug resistant cell lines of gastric cancer and pancreatic cancer to delineate the adaptive drug resistance mechanisms, and tested both in 3D cultured systems and in mice. We found several pathways, that are essential for regulation of cell stemness, are also involved in drug resistance. The relevance of our results to human cancer patients was confirmed in the TCGA data sets.

Xuefeng Chen – Wuhan University College of Life Sciences
Bre1-dependent H2B ubiquitination promotes homologous recombination by stimulating histone eviction at DNA breaks
DNA double-strand breaks (DSBs) are potent cytotoxic DNA lesion challenging genome stability that must be repaired faithfully to prevent cell death or tumorigenesis. Repair of DSBs requires eviction of the histones around DNA breaks to allow the loading of numerous repair and checkpoint proteins. However, the mechanism and regulation of this process remain poorly understood. Here, we show that histone H2B ubiquitination(uH2B) promotes histone eviction at DSBs independent of resection or ATP-dependent chromatin remodelers. Cells lacking uH2B or its E3 ubiquitin ligase Bre1 exhibit hyper-resection due to the loss of H3K79 methylation that recruits Rad9, a known negative regulator of resection. Unexpectedly, despite excessive single-strand DNA being produced, *bre1Δ* cells show defective RPA and Rad51 recruitment and impaired repair by homologous recombination and response to DNA damage. The HR defect in *bre1Δ* cells correlates with impaired histone loss at DSBs and can be largely rescued by depletion of CAF-1, a histone chaperone depositing histones H3-H4. Overexpression of Rad51 also partially suppresses the recombination defects of *bre1Δ* mutant. Thus, we propose that Bre1 mediated-uH2B promotes DSB repair through facilitating histone eviction and subsequent loading of repair proteins.

Min Dong, Boston Children's Hospital / Harvard Medical School
Turning bacterial toxins into therapeutics – developing a toxin-derived Wnt signaling inhibitor
Clostridium difficile infection (CDI) is the most common cause of antibiotic-associated diarrhea and gastroenteritis-associated death across developed countries. C. difficile toxin B (TcdB) is a major virulent factor responsible for diseases associated with CDI. The Wnt receptor frizzled protein family (FZDs) have been identified as major receptors for TcdB in the colonic epithelium. TcdB binds to the conserved Wnt-binding region of FZDs known as cysteine-rich domain (CRD), with the highest affinity toward FZD1, 2, and 7. The crystal structure of a TcdB fragment in complex with human FZD2 reveals an endogenous FZD-bound fatty acid acting as a co-receptor for TcdB binding. This lipid occupies the binding-site for Wnt-adducted palmitoleic acid in FZDs. TcdB binding locks the lipid in place, thereby preventing Wnt from engaging FZDs and signaling. Utilizing the ability of the FZD-binding domain of TcdB (TcdB-FBD) to effectively inhibit Wnt signaling, we showed that TcdB-FBD suppresses growth of triple-negative breast cancer in vivo by targeting FZD7 positive tumor initiating cells, thereby serving as a potential therapeutic protein.

Jian Lu – Peking University
Decreased Biosynthetic Energy Cost for Amino Acids in Cancer Evolution
Rapidly proliferating cancer cells have much higher demand for proteinogenic amino acids than normal cells. The use of amino acids in human proteomes is largely affected by their bioavailability, which is constrained by the biosynthetic energy cost in the living organisms. Conceptually distinct from gene-based analyses, we introduce the energy cost per amino

acid (ECPA) to quantitatively characterize the use of 20 amino acids during protein synthesis in human cells. By analyzing gene expression data from The Cancer Genome Atlas, we find that cancer cells evolve to utilize amino acids more economically by optimizing gene expression profiles. We further validate this pattern in an experimental evolution of xenograft tumors. ECPA not only shows robust prognostic power across many cancer types, but also improves the prediction of tumor response to checkpoint inhibitor immunotherapy. Our ECPA analysis reveals a common principle during cancer evolution.

Yan Yan – Hong Kong University of Science and Technology
The Drosophila scribble mutant cells display evolving properties during tumor progression

Loss of epithelial cell structure caused by cell polarity complexes has also been linked with growth control. The members of the Scribble cell polarity complex were originally discovered in Drosophila as “neoplastic tumor suppressor genes” (nTSGs). Drosophila larvae homozygous mutant for any of the nTSGs grow into giant larvae with tumorous imaginal discs and optic lobes. These mutant tumors fail to differentiate and grow into masses that survive serial transplantations, induce cachexia and eventually kill the hosts. Studies of the Drosophila nTSGs have provided valuable insights into the mechanisms of growth control and tumorigenesis. Interestingly, while the fly nTSG mutant tumors have successfully modeled many aspects of human epithelial cancers, it was noted that for the fly nTSG tumors that progress rapidly over days, a single gene mutation is sufficient to cause tumorigenesis, contrary to human tumors which supported a multiple-hit model and display a variable degree of genetic and epigenetic intratumor heterogeneity (ITH) that provides a foundation for selection and tumor evolution. Whether the rapid-developing fly nTSG tumor also exhibits a certain degree of intratumor heterogeneity and evolution capacity has remained unclear. We performed quantitative analysis of the scrib mutant tumor growth and found that the scrib mutant tumors display different growth rates and cell cycle profiles over time. Moreover, multiple growth-regulatory signaling pathway activities display quantitative differences in early and late scrib mutant tumors. Our data suggest that the scrib mutant cells undergo a transition from a growth arrest state to a proliferative state. Through longitudinal single cell RNA data analysis, we found that a combinatorial code of quantitative JNK, EGFR and Hippo signals can be used to define the proliferative states of individual cells. Moreover, the scrib mutant tumors harbor heterogeneous cell populations of different proliferative states, providing a foundation for possible selection and transition from an arrest state to a proliferation state as a population over time. This study provides the possibility of studying tumor evolution in a genetically accessible and fast-growing invertebrate tumor model.

Ping Ao – Shanghai Jiaotong University, Shanghai, China
Systems Biology Approach: endogenous network theory for normal and abnormal developmental dynamical processes

It is the right time to give new thoughts on cancer research a due opportunity. Starting around the turn of century, after many years working on cancer and related biological phenomena, two things became clear to us: cancer must be a systems biology phenomenon and the dominating somatic mutation theory has serious drawbacks. We began to formulate a new perspective on cancer genesis and progression, tentatively named endogenous network theory (ENT). Its first systematical exposition was made public in 2007. Subsequently I was invited to give it a presentation at the CBIS meeting at San Diego. Nearly 10 years later, ENT has passed its first stage development and begun to interact with experimental and clinical data, mainly due to my students and collaborators in China. During this time period, the biological power of ENT has been manifested from a different angle, for example, it has completely anticipated 4 additional hallmarks of cancer discussed in the celebrated 2011 Cell of Hanahan and Weinberg. Also, ENT has showed that cell types and lineages can be computed and predicted, very different from the current biological thinking,

and, beyond what advocated by those in the Human Cell Atlas. In my presentation I will give a demonstration of such long, difficult and persistent development, explain the key concepts behind this new approach to cancer, beyond “cancer as a disease of genetics”. I wish to stress the importance of quantitative and mechanism study in the future of biological and medical research and application. Two of our non-technical essays may also be helpful to understand the essence of ENT.

Recipients of CBIS 2018 Awards

The Chinese Biological Investigators Society (CBIS) is pleased to announce the recipients of this year's Ray Wu Award, Young Investigator Award, and Teaching award.

Ray Wu Award was established by the society to honor the late Dr. Ray Wu, who not only had a distinguished scientific career but also nurtured a new generation of Chinese scientists in life sciences through his tireless effort in promoting scientific and educational exchanges between China and the United States. The Award recognizes CBIS members who have made fundamental discoveries in life sciences and/or significant contributions in promoting life sciences in China. This year's recipients are:

Dr. Zhijian 'James' Chen, Ph.D., Investigator of Howard Hughes Medical Institute, George MacGregor Distinguished Chair in Biomedical Sciences, Director of Center for Inflammation Research, Professor of Department of Molecular Biology, University of Texas Southwestern Medical Center, for his pioneer work in deciphering the mechanisms and pathways of cell signaling, inflammation, and innate immunity, and for his discovery of cGAS in attracting drug target for treating autoimmune diseases and implicated cGAMP as a potential immuno-therapeutic or vaccine adjuvant.

Dr. Xinnian Dong, **Ph.D**., HHMI investigator, Professor of Biology, Duke University, for her discovery of a new component of nuclear pore complex (NPC) uncovered immune-induced NPC permeabilization as a novel molecular mechanism behind programmed cell death in eukaryotic cells, and her pioneer work on the interplay between the circadian clock and the metabolic rhythm in the context of plant immunity.

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CBIS/Science China – Life Sciences《中国科学-生命科学》Young Investigator Award recognizes CBIS members who are in the early career stages but have already made remarkable contributions in their respective fields. This year's awardees are:

Dr. Kun Zhang, PhD., Professor and chair of the Department of Bioengineering, University of California, San Diego, for his work in whole genome shotgun sequencing, single-cell sequencing methodologies for analyzing mammalian genomes, transcriptomes and chromatin accessibility, single-cell neuronal map of the human adult brain, development of targeted sequencing methods for human genome and methylome in stem cell and cancer research.

Dr. Zhihua Liu, **Ph.D**., Professor of the CAS Key Laboratory of Infection and Immunity Institute of Biophysics, Chinese Academy of Sciences, for her work in microbial derivatives that directly regulate intracellular membrane trafficking in the intestine and extra-intestinal organs, which may contribute to the broad physiological roles of microbiota, and the underlying molecular mechanisms for microbiota regulation to host physiology.

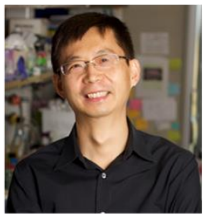
****

CBIS Teaching Award recognizes a CBIS member who has contributed extraordinarily to education in biomedical sciences, particularly in China. This year's awardee is:

Dr. Liqun Luo, **Ph.D**., Professor of Biology, Stanford University, and HHMI Investigator of Howard Hughes Medical Institute, for his contribution to neuroscience education in China.

Awardee Biographies

Dr. Zhijian 'James' Chen, **Ph.D.** – see plenary speaker biography (page 49)
Dr. Xinnian Dong, **Ph.D**. – see plenary speaker biography (page 50)
Dr. Liqun Luo, **Ph.D**. – see plenary speaker biography (page 41)



Kun Zhang, PhD
Professor and Chair
Department of Bioengineering
University of California at San Diego, CA, USA
E-mail: kzhang@bioeng.ucsd.edu

Kun Zhang received a B.S. from Fudan University in 1996, Ph.D. from the University of Texas Houston Health Science Center/MD Anderson Cancer Center in 2003, and did postdoctoral work at the Harvard Medical School. He joined the faculty of UCSD Bioengineering as an Assistant Professor in 2007, and was promoted to Full Professor in 2015. He started to serve as the Department Chair in 2018.

Zhang made important contributions to the field of genomics, especially on targeted sequencing and single-cell genomics. He demonstrated the first whole genome sequencing on single microbial cells in 2006, developed the first multiplexed targeted methylation sequencing method in 2009, and published the first single-cell neuronal maps of human adult brain in 2016. His group continues to develop molecular techniques and engineering platforms for building single-cell maps of multiple human organs.

He was named as a Rising New Investigator by Genome Technology in 2007, and elected into the AIMBE's College of Fellows in 2017.

Zhihua Liu, PhD
Laboratory of Immunology and Infection
Institute of Biophysics
Chinese Academy of Sciences

Zhihua Liu received BS from Beijing University in 1999, PhD from Harvard University in 2006, and did postdoctoral work in National Institute of Allergy and Infectious Diseases, National Institutes of Medicine. She started her lab in the Laboratory of Immunology and Infection in Institute of Biophysics, Chinese Academy of Sciences in 2012.

Liu made important contributions to the field of reciprocal interactions between the host and microbes, especially the intestinal commensal bacteria. Her lab is interested in the crosstalk between commensal bacteria with intestinal and extra-intestinal organs. She discovered that intestinal commensal bacteria directly target intracellular membrane trafficking in intestinal and extra-intestinal organs to modulate host physiology.

She was named as a NN-CAS Great Wall professor in 2013.

CBIS Board Election Ballot 2018-2020

President, please select one.
O Yibin Kang, re-elect

O _____(fill in name)

Vice President, please select one.
O Yingzi Yang, re-elect

O _____(fill in name)

Board members, please select 9 below or add name here. _____(fill in name)

O Lingling Chen, re-elect

O Lin He, new elect

O Charlene Xiaoling Liao, re-elect

O Zhenkun Lou, new elect

O Zhimin (James) Lu, new elect

O Yijun Qi, re-elect

O Feng Shao, new elect

O Xin Sun, re-elect

O Yihong Wan, new elect

O Wei Xu, new elect

O Jing Yang, new elect

O Hongtao Yu, new elect

O Zhenyu Yue, re-elect

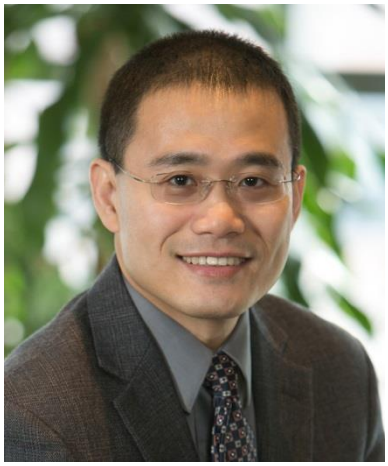
O Binhai Zheng, new elect

O Lee Zou, new elect

Please see following pages for each board candidate's personal statement

CBIS Board Member Candidate Statements

Yibin Kang, Ph.D.



Personal Statement

As a proud member of CBIS since I became an independent investigator in 2004, I have benefited from the support and guidance from many senior Chinese biologists. I also had the privilege to serve in the CBIS Board of Directors and as Vice President in the last four years. In seeking the re-election to the CBIS board and as President, I am committed to promoting the mission of CBIS, including helping the career development of young scientists, advancing the interest of the Chinese biological researchers (such as increasing our representation in AACR and other major conferences), connecting the academic and industrial research communities, and expanding the influence of CBIS in China.

Education

- 1991-1995 B.S. (Genetics) Fudan University, Shanghai, China (June, 1995)
- 1996-2000 Ph.D. (Genetics) Duke University, Durham, NC (May, 2000)
- 2000-2004 Postdoctoral Memorial Sloan-Kettering Cancer Center, NY

Positions and Employment

2004-2009 Assistant Professor
2010-2012 Associate Professor (tenured)
2012 Professor
2012- Warner-Lambert/Parke-Davis Professor of Molecular Biology (endowed)
Department of Molecular Biology, Princeton University, Princeton, NJ

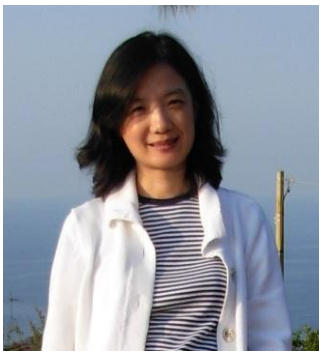
Awards and Honors

2006 Era of Hope Scholar Award, Department of Defense Breast Cancer Program
2011 The Vilcek Prize for Creative Promise in Biomedical Science
2012 AACR Award for Outstanding Achievement in Cancer Research
2013 Young Investigator Award, Chinese Biological Investigator Society
2014 Fidler Innovation Award, Metastasis Research Society
2014 Fuller Albright Award, American Society for Bone and Mineral Research
2014 AACR Outstanding Investigator Award in Breast Cancer Research
2016 Komen Scholar
2016 AAAS Fellow

Professional Services

2016-2018 President, Metastasis Research Society
2008-2012 Board of Directors, Metastasis Research Society
2018-2019 Chair, AACR Tumor Microenvironment Working Group
2014-2016 Research Task Force, Metastatic Breast Cancer Alliance
2013-2015 Board of Directors, Chinese Biological Investigator Society
2016-2018 Vice President, Chinese Biological Investigator Society
2011-2018 Scientific Committee, AACR Annual Meeting.

Yingzi Yang, Ph.D.



Personal Statement

My career growth has benefited from interacting with members of CBIS, for which I also have the distinct honor and privilege to serve as a member of the Board of Directors and as the Treasurer in the last four years. CBIS has provided a great platform for Chinese scientists to work together in promoting scientific excellence and political prominence. In seeking re-election as a CBIS Board member and Vice President, I am committed to contributing time and effort to extend the traditions of CBIS and hope my service can make us a stronger group in many aspects.

Education and Training:

1984-1988 B.S. Biophysics, Fudan University, Shanghai, China
1990-1996 Ph.D. Molecular Biology, Memorial Sloan Kettering Cancer Institute, New York City, NY
1996-2000 Postdoctoral fellow, Harvard University, Cambridge, MA

Positions:

2000-2006 Investigator, Head of the Developmental Genetics Section, National Human Genome Research Institute, NIH
2006-2014 Senior Investigator, Head of the Developmental Genetics Section, National Human Genome Research Institute, NIH
2015- Professor of Developmental Biology, Harvard School of Dental Medicine

Awards and honors

1995: Vincent du Vigneaud Award, Medical College of Cornell University
1996 Postdoctoral fellowship award from the Cancer Research Fund of the Damon Runyon-Walter Winchell Foundation.
2006: NIH Director's Seminar Series
2006: US Government Service Award
2006: NIH Award of Merit
2011: SCBA Young Investigator Award
2011: NIH APAO Outstanding Achievements and Merit Scholarship Award
2013: Keynote speaker at the NIH ceremony of Asian-American month

Professional Services

2012-2014, Member, NIH Central Tenure Committee
2016- Director, the BSDM DMD/ PhD Program, Harvard School of Dental Medicine
2017 Vice Chair, Cartilage biology and pathology Gordon Research Conference
2019 Chair, Cartilage biology and pathology Gordon Research Conference
2013-2018 Member of Board of Directors, Chinese Biological Investigator Society
2013-2018 Treasurer, Chinese Biological Investigator Society
2018- Associate Dean for Translational Research, Harvard School of Dental Medicine

Ling-Ling Chen, PhD

Personal Statement

If elected, I will work closely with CBIS presidents and other board members to carry forward the goal and mission of CBIS to facilitate scientific interaction and personal friendship among our members. Efforts will also be made to strengthen the connection and to stimulate scientific exchanges among CBIS members and beyond for collaboration and education.

Education/ Training

2000	BS (Biology)	Lanzhou University, Lanzhou, China
2003	MS (Pharmacology)	Shanghai Institute of Materia Medica, CAS, China
2009	PhD (Biomed)	UConn Health, USA
2009	MS (Management)	University of Connecticut, USA
2010	Postdoc fellow	UConn Health, USA

Positions and Employment

2010-2011	Assistant Professor in residence, UConn Health, USA
2011-	PI, Shanghai Institute of Biochemistry and Cell Biology, CAS
2017-	HHMI International Research Scholar

Services

2011- Journal Reviewer for Cell, Nature, Science, Cancer Cell, Mol Cell, Cell Stem Cell, Cell Metab, Cell Rep, Trends Biochem Sci, Trends Genet, Trends Neurosci, Nat Rev Genet, Nat Methods, Nat Genet, Genes Dev, Genome Res, Nat Commun, Cell Res, Genome Res, Genome Biol, J Cell Biol, RNA, Nucleic Acids Res, Mol Cell Biol and others.

2013- Member of CBIS; Member of ISSCR
2014- Editorial Board of Genome Biology
2015- Editorial Board of Trends in Genetics
2018- Editorial Board of Mobile DNA
2018- Editorial Board of RNA
2018- Life-long membership of the RNA Society

Selected Honors

2015 Li Ruqi Award from the Chinese Genetics Society
2016 CBIS Young Investigator Award
2016 Asian-Pacific Molecular Biology Network Young Investigator Award
2016 L'OREAL China for Women in Science
2017 National Science Foundation China Fund for Young Research Scholars
2017 C.C. Tan (Jia-Zhen Tan) Life Science Award
2017 Promega Innovation Award for Cell Biology
2018 Young Investigator Award of the Chinese Academy of Sciences
2018 National Program for Special Support of Eminent Professionals, China

Lin He, PhD

PERSONAL STATEMENT

As a member of the expanding community of life scientists of Chinese origin, I am seeking support to be elected on the CBIS board to serve our community. I am very interested in promoting the career development of young investigators of Chinese origin in North America, China and around the world, particular that of woman scientists who face more challenges in their career. I am also interested in fostering professional interactions among Chinese investigators and facilitating fruitful collaborations in interdisciplinary areas. Personally, I believe in the positive roles that professional organizations can play to build a collegial community, to promote better recognition of life scientists of Chinese origin, and facilitate fruitful collaboration.

EDUCATION:

09/1997-06/2003	Ph.D. Department of Genetics, Stanford University, Stanford, CA
09/1992-07/1997	B.S. Department of Biological Sciences and Biotechnology, Tsinghua University, Beijing, China

EMPLOYMENT HISTORY

07/2018-	Professor, MCB Department, Univ. of California – Berkeley
07/2014-	Associate professor, MCB Department, Univ. of California –Berkeley (tenured)
01/2008-06/2014	Assistant professor, MCB department, Univ. of California - Berkeley
09/2003-11/2007	Postdoctoral fellow with Dr. Greg Hannon, Cold Spring Harbor Laboratory

HONORS AND AWARDS

- Siebel Distinguished Chair professor 2018 - 2023
- Bakar Fellow 2017 - 2019
- HHMI Faculty Scholar Award 2016 - 2021
- Carcinogenesis Young Investigator Award 2014
- Hellman Fellow 2011
- MacArthur Fellow, MacArthur Foundation 2010 - 2014
- New Faculty Award, CIRM 2008 - 2013
- Searle Scholar, Kinship Foundation 2008 - 2011
- Pathway to independence award, NCI. 2007 - 2012
- Helen Hay Whitney Foundation Fellowship 2004 - 2007

Charlene Liao, PhD

Dr. Charlene Liao, a Genentech veteran with more than 20 years' experience as scientist and drug developer, is now President and CEO of Immune-Onc Therapeutics, Inc., an immuno-oncology startup developing innovative therapeutic antibodies for cancer treatment. Immune-Onc Therapeutics, Inc. won "Buzz of BIO" in 2017 and is named one of the top 20 Life Science Startups to Watch in 2018 by BioSpace.com.

Charlene Liao graduated from Peking University in China with a Biochemistry major. She was among 30 students of her year selected in China through the CUSBEA (China-United States Biochemistry Examination and Application) program to pursue Ph.D. in the United States. She holds Ph.D. in Biology from Brandeis University with Dr. Michael Rosbash (2017 Nobel Laureate), and conducted postdoctoral research in immunology at UCSF, first with Dr. Dan Littman, as a Fellow of the Damon Runyon Cancer Research Fund, and then with Dr. Art Weiss, as a Special Fellow of the Leukemia and Lymphoma Society of America. Since joining the industry and business world, Dr. Liao studied in the executive programs at Kellogg School of Management and at Stanford Graduate School of Business.

Dr. Liao began her bio-pharmaceutical industry career at Tularik Inc. (now Amgen) as a Scientist. Prior to joining Genentech Dr. Liao held various leadership positions at Rigel Inc., including Project Leader, Associate Director, and Director of Business Development. Dr. Liao joined Genentech in 2002 and has been a Project Team Leader since 2007. In near 14 years of her time at Genentech, Dr. Liao has contributed to numerous IND and/or CTA filings for 10 New Molecule Entities (NMEs) and has led drug development projects across therapeutic areas of oncology, immunology, neurology, inflammation, metabolic and infectious diseases. In 2016 Dr. Liao co-founded Immune-Onc Therapeutics, Inc. with Dr. Guo-Liang Yu and is serving as its President and CEO.

Dr. Liao has extensive leadership experience in non-profit organizations and served as their Board of Director or Executive Council/Committee Member:
Dr. Liao is currently on the Board of Directors of CBIS (Chinese Biological Investigators Society), elected in 2016. She has been responsible for the promotion and fundraising of the 2016 and 2018 CBIS meetings and has co-chaired or presented at the Entrepreneurship and Opportunities sessions in consecutive CBIS meetings. She has also organized CBIS-Industry sessions with local companies and governments of the city where the CBIS meeting took place.

Dr. Liao is one of the founding members and Board of Directors of the Ray Wu Memorial Fund (RWMF). RWMF works closely with other professional organizations such as CBIS (Chinese Biological Investigators Society) and SCBA (Society of Chinese Biologist in America), and awards the Ray Wu Prize to recognize excellence in life science research by a graduate student in an academic institution located in mainland China, Hong Kong, Taiwan, or Singapore. At a Board of Director of RWMF, Dr. Liao led strategic planning and fund-raising efforts, and led the development and launch of its official website (http://www.raywumemorialfund.org).

Dr. Liao served as Board of Director of PRISMS (Parents and Researchers Interested in Smith-Magenis Syndrome), an international patient supporting group that also sponsor research and foster partnerships with professionals.

Dr. Liao was an Executive Council member of the CABS (Chinese-American BioPharmaceutical Society), and Co-Chair of the Career and Business Development Committee. She initiated and led the Career Advisory Network (CAN) program to bring 1:1 mentorship to CABS members, which is in its 9th year. Currently, Dr. Liao is an Executive Committee Member of PKU Bio Teacher Fund that provides financial support for retired teachers of the College of Life Sciences (including those from the original Department of Biology) at Peking University, China.

Zhengkun Lou, Ph.D.

Personal Statement

Since its foundation, CBIS has done tremendous amount of work to facilitate the interactions of Chinese biologists throughout the world and promote life science in China. With the rapid advance of biological sciences and more and more Chinese investigators making important breakthroughs, CBIS provides a unique platform for the advancement of Chinese scientists. I am fully committed to the mission of CBIS and would make every effort to help with all the CBIS activities.

Education

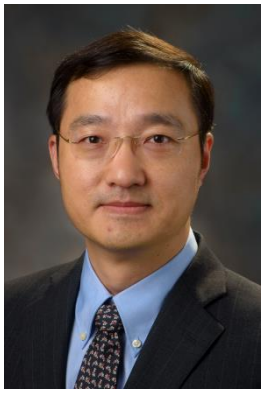
1988-1992 B.S. East China University of Science and Technology, China
1996-2001 Ph.D. Mayo College of Medicine, Rochester, MN
2001-2006 Postdoctoral Research Fellow, Department of Oncology, Mayo Medical Center.

Positions and Honors

2013- Professor, Department of Pharmacology, Mayo Clinic
2011- Co-Chair, Developmental Therapeutics Program, Mayo Clinic Cancer Center
2009-2012 Associate Professor, Department of Pharmacology, Mayo Clinic
2006-2009 Assistant Professor, Department of Pharmacology, Mayo Clinic.
1992-1995 Research Fellow, Shanghai Research Center for Biotechnology, Academia SINICA, Shanghai, China.

Editorial Board, Frontier in Radiation Oncology, 2011-
Editorial Board, J. Biol. Chem, 2014-
Editorial Board, Cancer Research, 2015-
President elect: American-China Association for Cancer Research, 2017
Susan G. Komen Research Award 2008
Fraternal Order of Eagles Cancer Research Award
Richard M Schultz Cancer Research Award, 2006-2011
Department of Defense Breast Cancer Research Fellowship 2003-2006

Zhimin Lu , M.D., Ph.D.



Personal Statement

I am an active member of Chinese biological and medical communities and actively serve CBIS. I have also participated in all major activities of SCBA (Society of Chinese Scientists in America) and many academic events in mainland of China, Hong Kong and Taiwen. After so many years' experience in academic research and endeavor to serve our communities, I have prepared myself ready and am willing to make more contribution to CBIS. I believe that CBIS will grow much stronger and become more influential under everybody's effort and that each of us will be benefited from CBIS for its support, its influence, and the opportunities that it creates.

Education

1981-1986	M.D	Taishan Medical College, China
1994-1999	Ph.D. (Biology)	The Graduate Center of the City University of New York
2000-2003	Postdoc	The Salk Institute

Position and Honors

Position

2003-2009, Assistant Professor, Department of Neuro-Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

2009-2013 Associate Professor, Department of Neuro-Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

2013-present Professor, Department of Neuro-Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

2015-present Ruby E. Rutherford Distinguished Professor, The University of Texas MD Anderson Cancer Center

Honors

1997 Beatrice Goldstein Konheim Graduate Scholarship in the Life Sciences, The City University of New York
1999 Pioneer Fund Fellowship, Salk Institute for Biological Studies
2000 California Breast Cancer Research Program Postdoctoral Fellowship
2007 Brain Tumor Society Program Award
2008 Peter Steck Memorial Young Investigator Award
2009 American Cancer Society Research Scholar
2012 Faculty Scholar Award, The University of Texas MD Anderson Cancer Center
2012 James S. McDonnell Foundation Scholar Award
2013 Potu N. Rao Award for Excellence in Basic Science, MD Anderson Cancer
2015 Center
2015 The Ruby E. Rutherford Distinguished Professorship, MD Anderson Cancer
2016 Center
University of Texas STARs Award
2017 The Dallas/Fort Worth Living Legend Faculty Achievement Award in Basic Research, MD Anderson
Cancer Center
American Association for the Advancement of Science Fellow

Yijun Qi, Ph. D

Center for Plant Biology
School of Life Sciences
Tsinghua University
Beijing 100084
China
Tel.: 86-10-62793132
Email: qiyijun@tsinghua.edu.cn

EDUCATION

Degree	Year	Major	Institution
h.D.	1998-2001	Plant Virology	Institute of Biotechnology, Zhejiang University
M.S.	1995-1998	Plant Virology	Institute of Biotechnology, Zhejiang Agricultural University
B.S.	1991-1995	Plant Pathology	Department of Plant Protection, Nanjing Agricultural University

PROFESSIONAL APPOINTMENTS

Year	Position	Institution
2016-present	Vice Dean	School of Life Sciences, Tsinghua University
2015-present	Professor	School of Life Sciences, Tsinghua University
2013-present	Director	Center for Plant Biology, Tsinghua University
2011-2015	Tenure-track Associate Professor	School of Life Sciences, Tsinghua University
2011-present	Investigator	Tsinghua-Peking Joint Center for Life Science (CLS)
2010-2011	Associate Investigator	National Institute of Biological Sciences, Beijing
2006-2010	Assistant Investigator	National Institute of Biological Sciences, Beijing
2004-2006	Postdoctoral Researcher	Cold Spring Harbor Laboratory
2001-2004	Postdoctoral Researcher	Department of Plant Biology, Ohio State University

RESEARCH INTERESTS

Mechanisms and functions of small RNAs in plants
Mechanisms and functions of long non-coding RNAs in plants

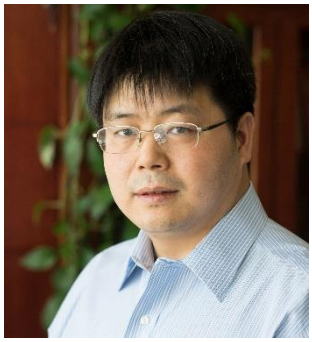
HONORS AND AWARDS

Year	Honors and awards
2017	National Innovation Award
2016	National Natural Science Award (the Second Prize)
2013	National Youth Science and Technology Award
2012	Recipient of The National Science Fund for Distinguished Young Scholars
2011	Changjiang Scholar, Ministry of Education of China
2010	Tanjiazhen Life Science Innovation Award

EDITORIAL ACTIVITIES

Year	Position	Journal
2017-present	Guest Editor	The Plant Cell
2016-present	Board of Reviewing Editor	eLife
2013-present	Editorial Board Member	Chromosoma: Biology of the Nucleus
2013-present	Editorial Board Member	Science China Life Sciences
2012-present	Associate Editor	Molecular Plant

Feng Shao, Ph.D.



Personal Statement

I was brought into the CBIS community (then Ray Wu Society) in 2005 right after I became an independent investigator at National Institute of Biological Sciences (NIBS), Beijing. Since then, I have participated many of the CBIS activities and got the opportunities to interact with many senior Chinese biologists, through which I received lots of supports and guidance to my career development. In seeking the election into the CBIS board, I am committed to fulfilling the mission of CBIS, including helping the career development of young scientists, increasing the presence and influence of the CBIS among the young generation of overseas returnee biologists in China, and promoting training and education of the next generation of Chinese biomedical scientists.

Education

• 1991-1996 B.S. (Applied Chemistry) Peking University, China
• 1996-1999 M.S. (Molecular Biology) Institute of Biophysics, CAS, China
• 1999-2003 Ph.D. (Biological Chemistry) University of Michigan, Ann Arbor, MI
• 2004-2005 Damon Runyon Postdoctoral Fellow Harvard Medical School, Boston, MA

Positions and Employment

2005-2009 Assistant Investigator, NIBS, Beijing
2009-2012 Associate Investigator, NIBS, Beijing
2012- Investigator, NIBS, Beijing
2014- Deputy Director for Academic Affairs, NIBS, Beijing

Awards and Honors

2008 The Zhou Guang Zhao Prize for Outstanding Youth in Basic Science
2012 HHMI International Early Career Award
2013 The Protein Society Irving Sigal Young Investigator Award
2013 The CBIS Young Investigator Award
2014 The Wu Jieping-Paul Janssen Medical & Pharmaceutical Award
2016 The FAOBMB Award for Research Excellence
2016 The Ho Leung Ho Lee Foundation Award for Science & Technology Progress
2017 The SCBA Kenneth Fong Young Investigator Award,
2017 Chinese Society of Cell Biology Outstanding Accomplishment Award

Members and Committes

2015- Member, Chinese Academy of Sciences
2015- Associate member, The European Molecular Biology Organization (EMBO)
2016- Fellow, American Academy of Microbiology
2015- Board of Directors, The Ray Wu Memorial Fund
2017- Council Member, China Postdoctoral Science Foundation (中国博士后科学基金会)
2017- Scientific advisor, Life Science Division of NSFC (国家自然科学基金委员会)
2017- Vice President, Beijing Western Returned Scholars Association (北京市欧美同学会)
2018- Council Member, Beijing Overseas Talents Association (北京海外高层次人才协会)
2018- Member, The National Committee of Science and Technology Awards (国家科学技术奖励委员会)

Xin Sun, Ph.D.

Personal Statement

My lab studies disease mechanisms using genomic and genetic approaches in mice. I was trained in *Drosophila* genetics, and later in mice genetics. Over the years, I have worked on many signaling pathways such as Notch and FGF, and many developmental processes, including fly wing and eye disc development, mouse gastrulation, somitogenesis and limb patterning. I established my lab at University of Wisconsin-Madison in 2002, and moved to UCSD in 2016. We investigate an array of lung developmental processes and their links to lung diseases. Since 2007, I have devoted time each year to teach in China, both at the graduate level as well as at the undergraduate level. In the US, I served for four years (2011-2014) as Director of the Cold Spring Harbor Laboratory summer course on Mouse Development, Stem Cells and Cancer, a flagship course for the Mouse research field. I have enjoyed serving on the CBIS board, and would like to use my organizational experience to work with the CBIS Chair and other board members to establish a functional platform for scientific exchange between researchers in and outside of China.

Education and Training

1985-1989 B.S. Biochemistry, Fudan University.
1990-1996 Ph.D. dissertation with Dr. Spyros Artavanis-Tsakonas at Yale University.
1997-2002 Postdoctoral research with Dr. Gail Martin at UCSF.

Positions

2002-2009 Assistant Professor, Laboratory of Genetics, University of Wisconsin-Madison.
2010-2013 Associate Professor, Laboratory of Genetics, University of Wisconsin-Madison.
2014-2016 Professor, Laboratory of Genetics, University of Wisconsin-Madison.
2016-now Professor, Department of Pediatrics, University of California, San Diego.

Honors and Services

2015-2021 NIH Lung Injury and Repair study section regular member.
2018 Organizer, Keystone on Endoderm Development and Disease.
2015 Romnes Faculty Fellowship, distinguished faculty award, University of Wisconsin.
2017-now WIRES Associate Editor.
2013-now Editorial board, Developmental Biology.
2005-now Editorial board, Developmental Dynamics.
2011-2014 Director of Cold Spring Harbor Laboratory summer course on Mouse Stem Cells, Development and Cancer.
2005-2007 Wisconsin Partnership Fund for a Healthy Future new investigator award.
2003-2005 March of Dimes Basil O'Conner award.
2001-2005 Burroughs-Wellcome career award.

Recent Selected Publications

Sui P, Wiesner DL, Xu J, Zhang Y, Lee J, Van Dyken S, Lashua A, Yu C, Klein BS, Locksley RM, Deutsch G, **Sun X**. Pulmonary neuroendocrine cells amplify allergic asthma responses. Science. 8;360(6393). pii: eaan8546.

Dai HQ, Wang, BA, Yang L, Chen JJ, Zhu GC, Sun ML, Ge H, Wang R, Chapman DL, Fuchou Tang FC, **Sun X***, Xu GL*. Tet-mediated DNA demethylation controls gastrulation by regulating Lefty-Nodal signaling. ***Nature***, 2016 Oct 538(7626):528-532. *Co-corresponding authors.

Branchfield K, Nantie L, Verheyden JM, Sui P, Wienhold MD, **Sun X.** Pulmonary neuroendocrine cells function as airway sensors to control lung immune response. ***Science.*** 2016 Feb, 351:707-10.

Yihong Wan, PhD

Personal Statement

CBIS is an excellent platform to meet new colleagues and friends. If elected, I will contribute to the goal and mission of CBIS by facilitating scientific interaction and personal friendship among our members. Working with CBIS presidents and other board members, I will promote scientific collaboration and educational exchange among Chinese scientists worldwide. These efforts will significantly benefit our community and strengthen the tradition of CBIS.

Education/Training

1994 BS (Biochemistry) Nankai University, Tianjin, China
1996 MS (Genetics) Southern Illinois University, Carbondale, IL, USA
2002 PhD (Molecular Biology) University of Colorado HSC, Denver, CO, USA
2008 Postdoc (Mol. Genetics) The Salk Institute, La Jolla, CA, USA

Positions and Employment

1993-1994 Undergraduate Researcher with Dr. Dechang Gao, Institute of Molecular Biology, China
1994-1996 Graduate student with Dr. Thomas Schmidhauser, Southern Illinois University, IL
1996-2001 Graduate student with Dr. Steve Nordeen, Univ. of Colorado HSC, CO
2002-2008 Postdoctoral Research Associate with Dr. Ronald Evans, HHMI, Salk Institute, CA
2008-2015 Assistant Professor (tenure-track), Dept of Pharmacology, UT Southwestern Med Center
2015- Associate Professor with tenure, Dept of Pharmacology, UT Southwestern Med Center, TX
2012- Adjunct faculty, Texas A&M Health Science Center, TX

Services

2009- Journal Reviewer for Nature Medicine, Cell Metabolism, JCI, PNAS, Genes & Development, Endocrinology, Molecular Endocrinology, Molecular and Cellular Biology, Cell Reports etc.
2009- Grant Reviewer for Swiss National Science Foundation, NIDDK-Diabetic Complications Consortium, NIH Study Sections, (A*STAR) in Singapore, Geneva University Hospitals and Faculty of Medicine Research Foundation in Switzerland etc.
2012- Guest Associate Editor for PLoS Genetics and PNAS
2012- Consultant for GlaxoSmithKline, Amgen, COI Pharmaceuticals, Acerta Pharmaceuticals, Guidepoint Global at New York, The Longevity Fund at San Francisco

Honors

1990-1994 ZhangShiChang Distinguished Scholar Award, NanKai University, China
1999 Univ. of Colorado HSC scholarship for the Annual Meeting of The Endocrine Society
2002 Keystone Symposia scholarship for the meeting “Chromatin Structrue and Activity”
1999-2002 U.S. Dept. of Defense Breast Cancer Research Program predoctoral fellowship
2003-2005 American Cancer Society postdoctoral fellowship
2008 Best Abstract Award for “Salk Science Day & Faculty Symposium”
2008-2012 Becton Dickinson Biosciences Research Grant Award
2008-2012 Virginia Murchison Linthicum Scholar Award in Medical Research
2009 ASBMR John Haddad Young Investigator Award
2010-2012 March of Dimes Basil O’Connor Starter Scholar Research Award
2010-2016 Cancer Prevention and Research Institute of Texas Individual Investigator Award
2011 Eugenia Rosemberg Award from The Endocrine Society
2012 Protégé of The Academy of Medicine, Engineering and Science of Texas (TAMEST)
2013-2014 The Charles and Jane Pak Center Innovative Research Award
2013 Awardee of Leadership Emerging in Academic Departments (LEAD) Program at UTSW
2014-2016 The Mary Kay Foundation Grant Award
2014 First GSK Pre-DPAc (Discovery Partnerships with Academia) Award at UTSW
2015 UTSW Friends of the Cancer Center Award
2016- Lawrence Raisz Endowed Professor in Bone Cell Metabolism
2016- Advisory Panel for International Osteoimmunology Conference in Greece
2017- Elected Faculty Senator at UT Southwestern

Wei Xu, Ph.D.

Personal Statement

I enjoy the friendship and high quality scientific programs at CBIS meetings and look forward to the scientific serendipity inspired by communication with the leading scientists. The CBIS board members carry out the mission to enhance the professional interactions and collaboration within a diverse group of biologists representing many fields, which agrees with my intended contributions to the society. If elected, I will help strengthen and optimize the operation of the society to provide the best education and research platform to scientists, especially to young scientists abroad and in China. I will also work with other board members to enhance the influence of the society, to increase funding opportunities, and to promote translation of basic science discoveries to the clinic.

Education/Training

1987-1991	BS (Chemistry)	Peking University, Beijing, China
1991-1994	MS (Biophysics)	Institute of Biophysics, Academic Sinica, China
1994-1999	PhD (Biochemistry)	University of Iowa, Iowa City, USA
1999-2005	Postdoc	The Salk Institute for Biological Studies, La Jolla, USA

Positions

2005-2011 Assistant Professor, Department of Oncology, University of Wisconsin-Madison
2011-2014 Associate Professor, Department of Oncology, University of Wisconsin-Madison
2014- Professor, Department of Oncology, University of Wisconsin-Madison
2017- Marian A. Messerschmidt Professorship in Cancer Research

Honors and Services

Susan Komen Breast Cancer Foundation Spotlight, 2008
Shaw Scientist Award, 2008
DOD ERA of HOPE Scholar, 2010
Society of Toxicology Achievement Award, 2013
Villas Distinguished Achievement Professor, 2014
Member of the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) of NIEHS, 2014
Romnes Faculty Fellowship, University of Wisconsin, 2016
Marian A. Messerschmidt Professorship, 2017
American Association for Chinese in Toxicology (AACT) Distinguished Chinese Toxicologist Lectureship award, 2017
Midwest Regional Chapter of the Society of Toxicology Kenneth P. DuBois Award, 2017
President, Mid-West Regional Chapter of Society of Toxicology, 2018

Editorial Board Member, Chemical Research in Toxicology, 2009-present
Editorial Board Member, American Journal of Cancer Research, 2011-present
Editorial Board Member, PLOS One, 2013-
Editorial Board Member, Journal of Biological Chemistry, 2017-
NCI CBSS study section regular member, 2012-
Programmatic Review for Breakthrough Awards, Department of Defense, 2015-

Jing Yang, Ph.D.

Personal Statement

Throughout my scientific career, I have received generous guidance and support from many outstanding scientists and founding members of the CBIS society, including Dr. Xiao-Fan Wang, who served in my PhD thesis committee at Duke and Dr. Xiang-Dong Fu and Dr. Kun- Liang Guan, who are senior colleagues at UCSD. I not only benefited scientifically from these interactions, but also learned the value of building a collaborative scientific community for Chinese life science investigators. Therefore, I would like to serve on the CBIS board to aid the goal of the society to promote interactions and collaborations of all Chinese life scientists around the world. Importantly, I would like to expand the efforts of the society to establish a support network to promote the career development of next generation investigators in life sciences.

Education

1990-1994 B.S. (Biology) University of Science and Technology of China, Hefei, Anhui
1994-1999 Ph.D. (Molecular Cancer Biology) Duke University, Durham, NC
2000-2006 Postdoctoral Fellow (Cancer Biology) Whitehead Institute, Cambridge, MA

Positions

2006-2012 Assistant Professor,
2012-2016 Associate Professor,
2016- Professor,
Department of Pharmacology and Pediatrics, Moores Caner Center, Univ. of California, San Diego, School of Medicine, La Jolla, CA

Honors

2000-2003 Damon Runyon Postdoctoral Fellowship
2007-2009 Kimmel Scholar Award
2007-2012 NIH Director's New Innovators Award
2010-2015 American Cancer Society Research Scholar
2012-2015 The Hartwell Foundation Investigator
2015-2019 President of the EMT International Association
2016 The John J. Abel Award in Pharmacology from The American Society for Pharmacology and Experimental Therapeutics (ASPET)
2016 The Young Investigator Award from Metastasis Research Society

Hongtao Yu, Ph.D.

Personal Statement

I attended my first CBIS (then Ray Wu Society) meeting in 2000, soon after I started my own laboratory in Dallas. I was impressed by the quality of the scientific program, and equally importantly, drawn to the informal and personal interactions among society members, both senior and junior. Since then, I have been attending the CBIS meetings regularly and have become a lifetime member of the society. Some of my best scientific ideas have originated from casual conversations with friends and colleagues at these meetings. The friendships forged at the meetings have led to fruitful collaborations and joint grant applications. Overall, I have benefitted immensely from being a member of this vibrant community. If elected to serve on the board, I will do my best to continue and expand the wonderful tradition of inclusiveness at the society, to help foster interactions among its members, and to advocate for and promote the career development of junior Chinese investigators in life sciences.

Education

1986-1990	B.S. in Chemistry	Peking University, Beijing, China
1990-1995	Ph.D. in Chemistry	Harvard University, Cambridge, MA
1995-1999	Postdoctoral Fellow in Cell Biology	Harvard Medical School, Boston, MA

Positions

1999-2004	Assistant Professor, Michael L. Rosenberg Scholar in Biomedical Research, Department of Pharmacology, UT Southwestern Medical Center, Dallas, TX
2004-2008	Associate Professor, Department of Pharmacology, UT Southwestern Medical Center, Dallas, TX
2008-present	Professor, Department of Pharmacology, UT Southwestern Medical Center, Dallas, TX
2008-present	Investigator, Howard Hughes Medical Institute
2016-present	Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology

Honors

1995	Damon Runyon-Walter Winchell Postdoctoral Fellowship
1999	Damon Runyon Scholar Award
2000	Burroughs Wellcome New Investigator Award in Pharmacological Sciences
2000	Packard Fellowship for Science and Engineering
2003	Leukemia and Lymphoma Society Scholar Award
2003	W.M. Keck Distinguished Young Scholar Award
2004	Greater Dallas Asian American Chamber of Commerce Award in Science
2012	American Association for the Advancement of Science (AAAS) Fellow

Zhenyu Yue, PhD.

Personal Statement

My goal is to work closely with the CBIS President and other members of the Board and serve the CBIS community with my best effort in promoting CBIS traditions, culture and spirit to pursue the best quality of science that has benefited the entire Chinese scientific community. I will also bring my best knowledge and experience in cell biology and neurodegenerative disease research to the Board and help structure and organize our scientific activities (conferences, collaboration, and fund raising) and improve education of the next generation scientists.

Education and Training

1988 BS (Cell Biology)
1991 MS (Vertebrate Genetics)
1997 PhD (Biochem/mol. Biology) Postdoc (Mol. Neuroscience) Wuhan University
2003 Chinese Academy of Sciences, Rutgers/Robert Wood Johnson Rockefeller University

Positions

2000-2003 Postdoc/Research Associate, Howard Hughes Medical Institute, The Rockefeller University,
2004-2008 Assistant Professor, Department of Neurology/Neuroscience, Mount Sinai School of Medicine, New York, NY.
2004-present Adjunct Faculty member of The Rockefeller University, New York, NY.
2008-2013 Associate Professor, Department of Neurology, Mount Sinai School of Medicine, New York, NY.
2013-present Professor, Department of Neurology/Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY

Honors

1998-2001 Postdoc Fellow, Howard Hughes Medical Institute.
2008 Faculty Council Award for Academy Excellence, Mount Sinai School of Medicine, Aidekman Endowed Professorship
2013
2015 (5/13) Keynote speaker, Friedman Brain Institute, Mount Sinai
2015 (9/25) Keynote speaker, SfN Hudson-Berkshire Chapter, Albany,
2013 Honorary Professor, Xiangya School of Med., Central South University, Hunan Guest
2015- Professor, Tongji Med. College, HuaZhong Sci. and Tech. University, Wuhan Guest
2015- Professor, Wuhan University Medical College, Wuhan

Other Experience and Professional Memberships:

2012/10- NIH study section, CMND, Regular. NIH study section, CMND, Ad Hoc.
2011/06 NIH study section, special review panel for the ZES1 LWJ-J MI NIH study section, invited to MBPP Ad Hoc
2011 NIH study section, ZRG1 CNNT-Q (02) S Ad Hoc. NIH study section, ZRG1 CNNT-Q (02) S Ad Hoc. NIH special panel RC4, Ad Hoc.
2011/06 Parkinson Disease Foundation, Review committee, Scientific Advisory Board,
2010/10
2010/06
2010
2011-4/25/2011Beijing Univ-Hsing Hua University Joint Life Center, Grant Review Panel

Binhai Zheng, Ph.D.

Personal Statement

I have been a faculty member at UC San Diego since 2005, where I have risen through the ranks to tenured full professor. My research program focuses on the fundamental principles and molecular mechanisms of axon regeneration and repair in the adult mammalian CNS using mouse models of spinal cord injury. In addition to running my own research program, I direct a multiscale microscopy imaging core that serves the entire UCSD campus. I serve on the executive committee for our Neurosciences Graduate Program and also serve as the Neurobiology training area leader for our Biomedical Sciences Graduate Program.

As a scientist born and raised in China, I am enthusiastic about promoting the interest of Chinese biological investigators in the U.S., China and beyond. In the past, I have taught graduate classes at Shanghai Institute of Biological Sciences, Beida and Tsinghua; I have hosted students from Chinese institutions (USTC and Jiaoda); I have helped with faculty recruitment for Zheda; I regularly give talks at various meetings and symposiums in China such as a Xiangshan scientific meeting last October and an upcoming neural regeneration meeting in Guangzhou later this year. I am a lifetime CBIS member and, if selected to serve, very much look forward to working with other board members to advance the mission of CBIS. In recent years, UC San Diego has seen rapid growth of a vibrant and collegial Chinese biological investigator community that I am an integral part of and frequently draw wisdom from. It will be an honor to serve on the CBIS Board of Directors representing our local Chinese faculty.

Education

1988 – 1992 B.S. equivalent (Genetics) Fudan University, Shanghai, China
1992 – 1994 M.S. (Biology) University of Kentucky, Lexington, Kentucky
1994 – 1999 Ph.D. (Genetics) Baylor College of Medicine, Houston, Texas
2000 – 2004 Postdoc (Neuroscience) UCSF/Stanford/Genentech, Bay Area, California

Positions

2005 – 2010 Assistant Professor, Department of Neurosciences, UC San Diego
2010 – 2016 Associate Professor, Department of Neurosciences, UC San Diego
2014 – now Director, UC San Diego School of Medicine/Neuroscience Microscopy Imaging Core
2016 – now Professor, Department of Neurosciences, UC San Diego
2018 – now Research Biologist, VA San Diego Healthcare System

Professional Activities

Editorial board Restorative Neurology and Neuroscience, Neural Regeneration Research, Experimental Neurology
Review board Sam Schmidt Paralysis Foundation, Craig H. Neilsen Foundation
Meeting org. Two mini-symposiums (~1K attendance each) at Society for Neuroscience meetings,
Annual San Diego Neural Regeneration Symposium (since 2012)
Workshop X-prize Paralysis Visioneering, NIH/NICHD Scientific Vision on Plasticity, NIH/NEI Audacious Goals Initiative, NIH/NINDS Spinal Cord Injury FAIR Share Community
Journal review >40 journals, current focus: Neuron, Nature series, Experimental Neurology
Grant review >10 NIH study sections; other grant agencies around the world: USA, Canada, UK,Austria, France, Israel, Singapore, Hong Kong (invited: China, Germany)

Lee Zou, Ph.D.

Personal Statement

I am an active member of the community of Chinese bioscientists. In addition to my participation in CBIS activities, I have served on the leadership teams of SCBA (Society of Chinese Scientists in America) and BBB (Boston Biology and Biotechnology Association). These experiences have given me the opportunity to interact with many bioscientists of Chinese origin, and acquire leadership skills in operating academic and social events. Through these experiences, I have learned the importance of having a strong community of Chinese bioscientists in the U. S., China, and around the world. All of us, as individuals and as a group, will benefit from this community for its support, its influence, and the opportunities that it offers. I am motivated to serve the CBIS as a member of its board.

Education

1988-1992	B.S. (Biochemistry)	Sun Yet-Sen University, China
1992-1994	M.S. (Biochemistry)	Kansas State University
1994-1999	Ph.D. (Genetics)	Stony Brook University & Cold Spring Harbor Laboratory
2000-2004	Postdoc (Biochemistry)	Baylor College of Medicine and Harvard Medical School

Position and Honors

2017-	James and Patricia Poitras Endowed Chair in Cancer Research
2013-	Professor of Pathology, Harvard Medical School
2012-	Associate Scientific Director, Massachusetts General Hospital Cancer Center
2009-2013	Associate Professor of Pathology, Harvard Medical School
2004-2009	Assistant Professor of Pathology, Harvard Medical School
2000	Fayez Sarofim Fellow (named fellow), the Damon Runyon Cancer Research Fund
2001/2	The V. C. Joshi Memorial Award, Baylor College of Medicine
2004	The Smith Family New Investigator Award, the Medical Foundation
2005	V Scholar, the V Foundation for Cancer Research
2005	Young Investigator Award, Breast Cancer Alliance
2006	Isselbacher Scholar Award, Massachusetts General Hospital
2007	New Scholar in Aging, the Ellison Medical Foundation
2009	The One Hundred Award, MGH Cancer Center
2009	Member, Faculty of 1000
2011	Member, Editorial Board, Molecular and Cellular Biology
2011	Scholar, Leukemia & Lymphoma Society
2011	The Jim & Ann Orr MGH Research Scholar
2011	Senior Scholar in Aging, the Ellison Medical Foundation
2012	Member, Editorial Board, Journal of Biological Chemistry
2014	Member, Editorial Board, Molecular Cell
2015	The Kraft Prize for Translational Research
2016	James & Patricia Poitras Endowed Chair in Cancer Research, Massachusetts General Hospital
2016	Member, Editorial Board, Cancer Research
2017	Professor Ying-Lai Wang Memorial Lectureship, Society of Chinese Bio-scientists in America
2017	Secretary Elect, Society of Chinese Bioscientists in America

Current CBIS Board Members

(Serving from August, 2016 to December, 2018)

Hao Wu, PhD., President

Yibin Kang, Ph.D. Vice-President, Chair of CBIS award committee

Guo-Min Li, Ph.D., Secretary, Co-chair of meeting program committee

Yingzi Yang, Ph.D., Treasurer

Lingling Chen, Ph.D., Member of meeting program committee

Lei Li, Ph.D., Co-chair of meeting program committee

Charlene Xiaoling Liao, Ph.D, Chair of meeting promotions committee

Yijun Qi, Ph.D., Co-chair of board member election committee

Xin Sun, Ph.D., Member of meeting program committee

Zhengyu Yue, Ph.D., Member of meeting program committee

Yimin Zou, Ph.D., Co-chair of board member election committee

Meeting Sponsors

The late Dr. Ray Wu and his generous support to CBIS

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