2022 Chinese Biophysics Congress

Program

Dec 2-4, 2022

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The Biophysical Society of China

Institute of Biophysics, CAS

Co-Organized by:

Henan University

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会议日程

	2-Dec-2022	3-Dec-2022	4-Dec-2022
	Friday	**Saturday**	**Sunday**
8:30-11:30		8:30-8:45 Opening Ceremony	8:30-9:15 Plenary Lecture-4
		8:45-9:30 Plenary Lecture-1	
		9:30-10:15 Plenary Lecture-2	9:15-10:00 Plenary Lectur-5
		10:15-10:30 Coffee Break	10:00-10:15 Coffee Break
		10:30-11:15 Plenary Lecture-3	10:15-11:00 Plenary Lecture-6
11:30-12:00		11:30-12:40 Workshop-1	11:30-12:40 Workshop-2
12:00-13:00			
13:00-13:30	女科学家论坛 （13:00-20:30）	纳米酶：新一代模拟酶的机遇与挑战 中日联合论坛-非经典膜运输，创新性思维 代谢生物学-代谢与疾病发生 单细胞多组学技术前沿进展 听觉声电转导的关键离子通道和机制 生命的动态：从系综到单分子	Break
13:30-14:30			结构与计算生物学II 神经生物物理-环路和系统 创新纳米药物及其临床前研究的关键因素 分子稳态、信号传导与细胞衰老 亚细胞结构的可视化前沿 表型组学与人类健康 （含15分钟休息）
14:30-15:00			
15:00-16:00			
16:00-16:30		Break	
16:30-17:00		结构与计算生物学I 神经生物物理-细胞和分子 新一代纳米药物及人类健康 感染与免疫 体卫融合与低氧健康 生命的动态：从系综到单分子	
17:00-18:00			17:00-17:15 闭幕式
18:00-19:00			
19:00-19:30			

Scientific Program

Dec 2 (Friday)

Women Scientist Forum

Time	Schedule
13:30-20:30	Women Scientist Forum

Dec 3 (Saturday)

Opening Ceremony

Time	Schedule
8:30-8:45	Opening Ceremony

Plenary Lecture

Time	Speaker	Title/Affiliation	Page
8:45-9:30	Songling Wang	从口腔走向全身的健康使者-硝酸盐 *(Capital Medical University)*	22
9:30-10:15	Guozhi Liu	THz与生物物理 *（Academy of Military Sciences）*	23

Coffee Break

Time	Schedule
10:15-10:30	Coffee Break

Plenary Lecture

Time	Speaker	Title/Affiliation	Page
10:30-11:15	Ye Tian	Mitochondrial surveillance pathway mediates organismal aging *(Institute of Genetics and Developmental Biology, CAS)*	24

S11 纳米酶：新一代模拟酶的机遇与挑战 Nanozymes: the Opportunities and Challenges for Next Generation of Artificial Enzymes

Time: 3 Dec. 13:00-16:00

No	Time	Speaker	Title / Affiliation	Page
	13:00-16:00	Chairs:Xiyun Yan, Xiaogang Qu		
1	13:00-13:30	Ning Gu	铁基纳米酶 *(Southeast University, China)*	25
2	13:30-14:00	Xiaogang Qu	Construction of Bio-inspired Nanozymes and Their Applications *(Changchun Institute of Applied Chemistry, CAS)*	26
3	14:00-14:30	Zhiyong Tang	Self-assembly of porous nanomaterials for enzyme-mimicking catalysis *(National Center for Nanoscience and Technology, China)*	27
4	14:30-15:00	Lianbing Zhang	适冷纳米酶 *(Institute of Biophysics, CAS, China)*	28
5	15:00-15:30	Chengzhou Zhu	纳米酶原子尺度调控及其生物传感应用 *(Central China Normal University, China)*	29
6	15:30-16:00	Hui Wei	Nanozymes: from rational design and biomedical applications *(Nanjing University, China)*	30

S2 中日联合论坛-非经典膜运输，非经典功能/China-Japan Joint Session-Unconventional Membrane Trafficking, Innovative Thinking

Time: 3 Dec. 13:00-16:00

No	Time	Speaker	Title / Affiliation	Page
	13:00-16:00	Chairs: Anbing Shi, Masataka Yanagawa		
1	13:00-13:20	Yao Lu	Analysis of intercellular interactions with single-cell secretomic analysis microchip *(Dalian Institute of Chemical Physics, CAS, China)*	31
2	13:20-13:40	Yuji Hara	Role of the mechanosensing machinery in myogenesis *(University of Shizuoka, Japan)*	32
3	13:40-14:00	Min Zhang	Regulation of unconventional secretion by coronavirus factors *(Tsinghua University, China)*	33

4	14:00-14:20	Shunsuke F. Shimobayashi	Liquid phase condensation in living cells *(Kyoto University, Japan)*	34
5	14:20-14:35	Jianping Xu	Imaging method for membrane research *(Leica Microsystems)*	35
		14:35-15:00 Tea Break		
6	15:00-15:20	Long Lin	SMGL-1/NBAS acts as a RAB-8 GEF to regulate unconventional secretion *(Huazhong University of Science and Technology, China)*	36
7	15:20-15:40	Masataka Yanagawa	Single-molecule imaging analysis of G protein-coupled receptor signalosome *(RIKEN Cluster for Pioneering Research, Japan)*	37
8	15:40-16:00	Xiaohui Cang	Mechanistic Insights into Multiple-step Transport of Mitochondrial ADP/ATP Carrier *(Zhejiang University, China)*	38

S3 代谢生物学-代谢与疾病发生

Time: 3 Dec. 13:00-15:15

No	Time	Speaker	Title / Affiliation	Page
	13:00-16:00	Chairs: Jiansheng Kang, Xiwen Xiong		
1	13:00-13:15	Hua Wang	衰老与酒精肝 *(Anhui Medical University, China)*	39
2	13:15-13:30	Mindian Li	限时进食改善骨骼肌功能的分子机制 *(The Southwest Hospital of AUM, China)*	40
3	13:30-13:45	Zhihong Xue	Metabolic enzymes moonlighting as RNA binding proteins *(Sichuan University, China)*	41
4	13:45-14:00	Yang Xiang	Centenarian genetic variations contribute to longevity by metabolic reprogramming *(Nanchang University, China)*	42
5	14:00-14:15	Jin Li	肠道-代谢稳态调控的新视角 *(Second Hospital of Shanxi Medical University, China)*	43
6	14:15-14:30	Jianling Zhao	细胞空间站-亚细胞结构成像探索 *(Carl Zeiss (Shanghai) Co.,Ltd)*	44
7	14:30-14:45	Feng Rao	葡萄糖感知与代谢的蛋白质稳态和转录调控 *(Southern University of Science and Technology)*	45

8	14: 45-15:00	Junli Liu	The Polymodal WAT Browning in Metabolism *(Shanghai Sixth People's Hospital)*	46
9	15:00-15:15	Youkun Bi	Bone marrow derived-mesenchymal stem cell improves diabetes-associated fatty liver via mitochondria transformation in mice *（Institute of Biophysics, CAS, China）*	47

S14 单细胞多组学技术前沿进展/Single-Cell Multiomics Technologies

Time: 3 Dec. 13:00-16:00

No	Time	Speaker	Title / Affiliation	Page
	13:00-16:00	Chairs:Xiaoqun Wang, Fuchou Tang		
1	13:00-13:30	Tian Xue	Single cell atlas of the aging and light/dark-adapted retina *(University of Science and Technology of China)*	48
2	13:30-14:00	Chen Wu	TBD *(Peking Union Medical College, China)*	49
3	14:00-14:30	Xin Zhou	Spatial-temporal transcriptional landscape of mammalian hypothalamus development *(Beijing Normal University, China)*	50
4	14:30-15:00	Jianbin Wang	多维度单细胞分析技术 *(Tsinghua University, China)*	51
5	15:00-15:30	Jia Yu	Single-cell architecture and functional requirement of lncRNA and alternative splicing during hematopoietic stem cell formation *(Chinese Academy of Medical Sciences)*	52
6	15:30-16:00	Ji Dong	Decoding the molecular mechanisms of ultrasound perception in bat auditory cortex *(Bioland Laboratory, China)*	53

S5 听觉声电转导的关键离子通道和机制

Time: 3 Dec. 13:00-15:55

No	Time	Speaker	Title / Affiliation	Page
	13:00-15:55	Chairs: Zhiqiang Yan, Fanglei Ye		
1	13:00-13:25	Lijun Kang	TMC Proteins Modulate Membrane Excitability through a Background Leak Conductance *(Zhejiang University, China)*	54

2	13:25-13:50	Fanglei Ye	人工耳蜗植入的听觉生理基础 *(The First Affiliated Hospital of Zhengzhou University)*	55
3	13:50-13:15	Zhiqiang Yan	TMC1 and TMC2 Proteins Are Pore-Forming Subunits of Mechanosensitive Ion Channels *(Shenzhen Bay Laboratory)*	56
4	14:15-14:40	Zhigang Xu	FCHSD2 is required for stereocilia maintenance and hearing *(Shandong University, China)*	57
5	14:40-15:05	Yiquan Tang	TMC机械转导通道上膜转运的分子机制 *(Fudan University,China)*	58
6	15:05-15:30	Yu Lu	基于耳聋基因变异数据的听觉基因功能和分子机制研究 *(West China Hospital of Sichuan University, China)*	59
7	15:30-15:55	Zuhong He	核转录因子FoxG1在老年性聋发生发展中的作用机制研究 *(Zhongnan Hospital of Wuhan University, China)*	60

S4 生命的动态: 从系综到单分子/Dynamics of Life: Correlating Ensemble and Single Molecule Levels

Time: 3 Dec. 13:00-17:40

No	Time	Speaker	Title / Affiliation	Page
	13:00-18:00	Chairs: Xuncheng Su, Xuefeng Guo		
1	13:00-13:20	Zheng Liu	Lighting up the mechanical forces in living cells at the single-molecule level *(Wuhan University, China)*	61
2	13:20-13:40	Wei Chen	新冠病毒刺突的力学激活机制及阻断策略 *(Zhejiang University, China)*	62
3	13:40-14:00	Zhongbo Yu	TRF1动态组织一条端粒DNA的单分子机制 *（Nankai University，China)*	63
4	14:00-14:20	Shuo Huang	仿生孔道纳米孔化学：从原子到生命 *（Nanjing University, China)*	64
5	14:20-14:40	Xinghua Zhang	DNA甲基化促进促进同源重组 *(Wuhan University, China)*	65
6	14:40-15:00	Xianyang Fang	Regulatory mechanisms of mechanical anisotropy and conformational dynamics of flaviviral xrRNAs by single-molecule techniques *(Institute of Biophysics, CAS)*	66

7	15:00-15:10	Lei Zeng	BRD4-NUT融合蛋白在p300激活的超乙酰化中的结构机制 *（First Hospital of Jilin University, China）*	67
15:10-15:40 Tea Break				
8	15:40-16:00	Yajun Jiang	Molecular Chaperones in Action *（Nanjing University, China）*	68
9	16:00-16:20	Shenlin Wang	RNA的固体核磁共振研究新方法 *（East China University of Science and Technology）*	69
10	16:20-16:40	Junxia Lu	固态核磁研究细胞坏死调控中重要功能性纤维蛋白结构 *（ShanghaiTech University, China）*	70
11	16:40-17:00	Chaowei Shi	The fluoride permeation mechanism of the fluc channel revealed by solid-state NMR *（University of Science and Technology of China）*	71
12	17:00-17:20	Yin Yang	生物大分子中的高分辨DEER距离测量 *（Nankai University，China）*	72
13	17:20-17:30	Huijuan You	Nucleic acids structural dynamics and interactions with small ligands analyzed by single-molecule magnetic tweezers *（Huazhong University of Science and Technology）*	73
14	17:30-17:40	Peng Zheng	单分子力谱和分子模拟揭示新冠病毒N501Y突变提高病毒与受体间相互作用力及其分子机制 *（Nanjing University, China）*	74

S1-1 结构与计算生物学I/Structural and Computational Biology I

Time: 3 Dec. 16:30-19:15

No	Time	Speaker	Title / Affiliation	Page
	16:30-19:15	Chairs: Yihua Huang, Ning Gao		
1	16:30-16:50	Yao Cong	Molecular basis of receptor binding and antibody neutralization of Omicron *(Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, CAS, China)*	75
2	16:50-17:10	Haiyan Liu	基于统计能量以及深度学习的蛋白质设计 *(University of Science and Technology of China)*	76
3	17:10-17:30	Jinbiao Ma	Structural insights into ATP-dependent processing of long double-stranded RNAs by Drosophila	77

			Dicer-2/Loqs-PD complex *(Fudan University, China)*	
4	17:30-17:50	Shujia Zhu	NMDA receptors: from atomic structures to diverse physiological functions *(Institute of Neuroscience, CAS, China)*	78
5	17:50-18:00	Xiangli Wang	The Recent Advances and Application in Cryo-EM *（Thermo Fisher Scientific）*	79
6	18:00-18:15	Ju Zhou	Structural mechanism of GTP initiating microtubule assembly *(Tsinghua University, China)*	80
7	18:15-18:30	Yunlu Kang	Structure and mechanism of NALCN channel complex *(Peking University, China)*	81
8	18:30-18:45	Yunjie Zhao	Computational methods to regulate RNA functions *(Central China Normal University)*	82
9	18:45-19:00	Ge Yang	DeepETPicker: Fast and accurate 3D particle picking for cryo-electron tomography using weakly supervised deep learning *(Institute of Automation，CAS, China)*	83
10	19:00-19:15	Zongqiang Li	Near-atomic structure of the inner ring of the Saccharomyces cerevisiae nuclear pore complex (Tsinghua University, China)	84

S8 神经生物物理-细胞和分子/Neurobiophysics-Cell&Molecule

Time: 3 Dec. 16:30-18:30

No	Time	Speaker	Title / Affiliation	Page
	16:30-18:30	Chairs: Qian Liu, Shiqian Qi		
1	16:30-16:45	Jianwei Jiao	神经干细胞及脑发育疾病机理研究 *(Institute of Zoology,CAS, China)*	85
2	16:45-17:00	Xingguo Liu	线粒溶酶体（mitolysosome）胞吐：帕金森症线粒体质量控制新途径 *(Guangzhou Institutes of Biomedicine and Health, CAS,China)*	86
3	17:00-17:15	Renjie Chai	The potential application of Stem Cell transplantation in the Cochlear Implants *(Southeast University, China)*	87

4	17:15-17:30	Xiaojun Xu	UPRmt activation for the treatment of Parkinson's disease *(China Pharmaceutical University)*	88
5	17:30-17:45	Eryan Kong	The roles of protein palmitoylation in neurodegenerative diseases *(Xinxiang Medical University, China)*	89
6	17:45-18:00	Qiang Liu	阿尔茨海默症的表观遗传调控 *(University of Science and Technology of China)*	90
7	18:00-18:15	Shiqian Qi	The structure and function of ALS-linked C9orf72 complex *(West China Hospital，Sichuan University)*	91
8	18:15-18:30	Tong Xin	Hello, the era of intelligent microscopic imaging analysis *(Leica Microsystems)*	92

S7 新一代纳米药物及人类健康/New Generation Nanomedicine and Health

Time: 3 Dec. 16:15-19:40

No	Time	Speaker	Title / Affiliation	Page
	16:15-19:40	Chairs: Bingyang Shi, Meng Zheng		
1	16:15-16:35	Weibo Cai	(Cancer) Theranostics with Radiolabeled Nanomaterials *(University of Wisconsin–Madison, USA)*	93
2	16:35-16:55	Zhiyong Qian	可局部注射纳米药物研究进展 *(Sichuan University, China)*	94
3	16:55-17:15	Aiguo Wu	铁基纳米药物及其肿瘤诊治 *(Ningbo Institute of Materials Technology & Engineering, CAS, China)*	95
4	17:15-17:35	Cong Li	TBD *(Fudan University, China)*	96
5	17:35-17:55	Qiang Zhao	血管组织工程研究 *(Nankai University，China)*	97
6	17:55-18:15	Yongzhuo Huang	靶向肿瘤代谢/免疫互作的递药策略 *(Shanghai Institute of Materia Medica, CAS, Chinaa)*	98
7	18:15-18:30	Lichen Yin	大分子药物胞内递送系统 *(Soochow University, China)*	99
8	18:30-18:45	Lin Mei	纳米药物递送：从靶向到精准 *(Chinese Academy of Medical Science & Peking Union Medical College Institude of Biomedical Engineering)*	100
9	18:45-19:00	Xianzhu Yang	核酸药物的体内递送载体构建及应用研究 *(South China University of Technology, China)*	101

10	19:00-19:20	Michael Mitchell	Lipid Nanoparticle-Mediated mRNA Delivery for CAR T Cell Engoneering *(University of Pennsylvania, USA)*	102
11	19:20-19:40	Yizhou Dong	Development of Nanomaterials for mRNA Therapeutics, Genome Editing and Cell Therapy *(Ohio State University,USA)*	103

S13 感染与免疫/Infection and Immunity

Time: 3 Dec. 16:30-18:50

No	Time	Speaker	Title / Affiliation	Page
	16:30-18:50	Chairs:Guangxia Gao, Gong Cheng		
1	16:30-16:50	Chunhong Ma	HBV与宿主相互作用研究 *（Shandong University, China)*	104
2	16:50-17:10	Guoxin Liang	Vpr 通过拮抗限制性因子 LAPTM5 而促进 HIV 感染巨噬细胞 *（China Medical University）*	105
3	17:10-17:30	Mingzhou Chen	Vimentin inhibits α-tubulin acetylation via enhancing α-TAT1 degradation to suppress the replication of human parainfluenza virus type 3 *（Wuhan University, China）*	106
4	17:30-17:50	Jincun Zhao	Basic Research meets the Needs for Clinical Practice of Respiratory infectious Diseases *(First Affiliated Hospital of Guangzhou Medical University, China)*	107
5	17:50-18:10	Yi Zhang	新冠病毒感染免疫学特点和干预 *(Zhengzhou University , China)*	108
6	18:10-18:35	Gong Cheng	Skin microbiota, odorants and arbovirus transmission *(Tsinghua University, China)*	109
7	18:35-18:50	Shoudeng Chen	The molecular characterization of the highly immunogenic SARS-CoV-2 nucleocapsid protein *(Sun Yat-sen University, China)*	110

S10 体卫融合与低氧健康/The Integration of Sports and Public Health & Hypoxic Healthy

Time: 3 Dec. 16:30-19:10

No	Time	Speaker	Title / Affiliation	Page
	16:30-19:10	Chairs: Ru Wang, Dongya Yuan		
1	16:30-16:50	Hao Wu	A Comparative Study of Hypoxia, Hyperoxia and Exercise Health *(Capital University of Physical Education and Sports, China)*	111
2	16:50-17:10	Fuhai Ma	高原运动医学研究进展 *(Qinghai Institute of Sports Science, China)*	112
3	17:10-17:30	Junjie Xiao	保护心脏的“一石三鸟”效应 *(Shanghai University，China)*	113
4	17:30-17:50	Lan Zheng	以果蝇为模型：衰老心脏的运动健康促进研究 *(Hunan Normal University, China)*	114
5	17:50-18:10	Rui Chen	低氧诱导外泌体参与结直肠癌转移的机制探讨 *(Capital Medical University, China)*	115
6	18:10-18:25	Dianjianyi Sun	A Review of Epidemiological Studies on Genomic longevity and aging *(Peking University)*	116
7	18:25-18:40	Bingxiang Xu	Regulation of chromatin states and conformations during heat shock response in mammalian cells *(Shanghai University of Sport，China)*	117
8	18:40-18:55	Qian Di	The Joint Effect of PM2.5 Exposure and Physical Activity on Cognitive Function and Hemodynamic Response: A fNIRS study *(Tsinghua University，China)*	118
9	18:55-19:10	Xin Sun	A comparative study on the characteristics of plantar pressure of high altitude native and immigrant college students *(Xizang University, China)*	119

Dec 4 (Sunday)

Plenary Lecture

Time	Speaker	Title/Affiliation	Page
8:30-9:15	Guanghui Ma	仿生合成疫苗: 从人工颗粒到天然颗粒底盘 *(Institute of Process Engineering, CAS, China)*	120

9:15-10:00	Xiaoqun Wang	脑发育与演化的分子细胞调控机制 *(Beijing Normal University)*	121

Coffee Break

Time	Schedule
10:00-10:15	Coffee Break

Plenary Lecture

Time	Speaker	Title/Affiliation	Page
10:15-11:00	Maili Liu	TBD *(Innovation Academy for Precision Measurement Science and Technology, CAS)*	122

S1-2 结构与计算生物学-II/Structural and Computational Biology II

Time: 4 Dec. 13:30-16:43

No	Time	Speaker	Title / Affiliation	Page
	13:30-16:43	Chairs: Hongwei Wang, Pu Gao		
1	13:30-13:50	Zhiwei Huang	TBD *(Harbin Institute of Technology, China)*	123
2	13:50-14:05	Fan Yang	Structural mechanisms of TRPV2 modulation by endogenous and exogenous ligands *(Zhejiang University, China)*	124
3	14:05-14:20	Linhua Tai	Architecture of Outer Rings From Xenopus laevis Nuclear Pore Complex Obtained By Cryo-EM and AI *(Institute of Biophysics, CAS, China)*	125
4	14:20-14:35	Nan Liu	Keep your particles well-behaved: Graphene support to boost Cryo-EM analysis *(Tsinghua University, China)*	126
5	14:35-14:55	Jianping Wu	Cryo-EM study of CatSpermasome—a sperm channel-transporter supercomplex *(Westlake University, China)*	127
		14:55-15:10 Tea Break		
6	15:10-15:30	Jiamu Du	植物DNA去甲基化机制研究 *(Southern University of Science and Technology, China.)*	128

7	15:30-15:45	Qin Cao	Cryo-EM structures of TMEM106B fibrils extracted from FTLD-TDP patients *(Shanghai Jiao Tong University, China)*	129
8	15:45-16:00	Xin Yong	SNX proteins-mediated endosomal trafficking *(Tsinghua University, China)*	130
9	16:00-16:15	Hongxing He	A direct method to solve protein crystal structures from X-ray diffraction data with iterative projection and deep learning algorithms *(Ningbo University, China)*	131
10	16:15-16:35	Longxing Cao	General approach to design of miniprotein binders to arbitrary protein targets *(Westlake University, China)*	132
11	16:35-16:43	Peiwei Han	告别昂贵维护和浓度梯度-基于光栅耦合波导干涉的分子互作动力学分析技术 *（Malvern Panalytical）*	133

S8 神经生物物理学-环路和系统/Neurobiophysics-Circuit&System

Time: 4 Dec. 13:30-16:30

No	Time	Speaker	Title / Affiliation	Page
	13:30-16:30	Chairs: Peng Cao, Han Xu		
1	13:30-14:00	Xiaoming Li	情感和情感障碍的神经环路研究 *(Zhejiang University, China)*	134
2	14:00-14:30	Liping Wang	恐惧情绪与睡眠环路 *(Shenzhen Institutes of Advanced Technology, CAS, China)*	135
3	14:30-15:00	Zhi Zhang	靶向视觉系统调控疼痛的神经环路机制 *(University of Science and Technology of China)*	136
4	15:00-15:30	Zhihua Gao	下丘脑神经内分泌系统的结构与功能解析 *(Zhejiang University, China)*	137
5	15:30-16:00	Miao He	Combinatorial genetic dissection of neural circuits *(The Institutes of Brain Science, Fudan University, China)*	138
6	16:00-16:30	Cheng Zhan	A vagal-NTS pathway that stimulates feeding *(University of Science and Technology of China)*	139

S12 创新纳米药物及其临床前研究的关键因素/Nanomedicine Development and Key Factors for Pre-clinical Investigationsn

Time: 4 Dec. 13:30-16:45

No	Time	Speaker	Title / Affiliation	Page
	13:30-16:45	Chairs: Guangjun Nie, Daishun Ling		
1	13:30-13:55	Weiping Gao	Elastin-like polypeptide fused protein drugs *(Peking University, China)*	140
2	13:55-14:20	Xiaozhong Qiu	A Nanocomposite-based Vascularized Elastic Conductive Patch for the Repair of Infarcted Myocardium *(Southern Medical University, China)*	141
3	14:20-14:45	Jin Sun	前药自组装纳米药物在肿瘤治疗中的应用 *(Shenyang Pharmaceutical University, China)*	142
4	14:45-15:10	Zhanli Hu	动态PET定量成像技术 *(Shenzhen Institutes of Advanced Technology, CAS, China)*	143
		15:10-15:25 Tea Break		
5	15:25-15:50	Fangyuan Li	离子响应纳米探针 *(Zhejiang University, China)*	144
6	15:50-16:15	Yunlu Dai	金属多酚配位生物材料在癌症治疗领域的应用探索 *(University of Macau)*	145
7	16:15-16:30	Tao Wang	雄黄纳米晶在髓系白血病治疗中的应用及机理研究 *(Chinese Academy of Medical Sciences and Peking Union Medical College)*	146
8	16:30-16:45	Ye Liu	A new polysaccharide platform constructs self-adjuvant nanovaccines to enhance immune responsesy *(Institute of Medical Biology, Chinese Academy of Medical Sciences and Peking Union Medical College)*	147

S6 分子稳态、信号传导与细胞衰老的机制

Time: 4 Dec. 13:30-16:25

No	Time	Speaker	Title / Affiliation	Page
	13:30-16:25	Chairs: Junping Liu		
1	13:30-13:50	Jinqiu Zhou	Single-chromosome fission yeast models reveal the configuration robustness of a functional genome *(Center for Excellence in Molecular Cell Science, CAS, China)*	148
2	13:50-14:10	Xiaoli Tian	基因、环境与长寿 *(Nanchang University, China)*	149

3	14:10-14:30	Qingpeng Kong	Transcriptomic insights into the longevity factors in centenarians *(Kunming Institute of Zoology, CAS, China)*	150
4	14:30-14:50	Weiqi Zhang	Heterochronic parabiosis induces stem cell revitalization and systemic rejuvenation across aged tissues *(Beijing Institute of Genomics, CAS, China)*	151
5	14:50-15:10	Tangliang Li	mRNA质量控制与衰老的机制 *(Hangzhou Normal University, China)*	152
6	15:10-15:25	Deshun Gong	Structure of the human Meckel-Gruber protein Meckelin *（Nankai University，China）*	153
7	15:25-15:40	Hongyu Hu	Sequestration of cellular native factors by protein aggregates *(Center for Excellence in Molecular Cell Science, CAS, China)*	154
8	15:40-15:55	Peng Liu	PINK1 regulates Aβ and hyperphosphorylated tau induced mitophagy-lysosomal degradation, neuroinflammation, and oxidative stress *（Shenyang Pharmaceutical University, China）*	155
9	15:55-16:10	Hong Zhang	Chaperone codes of Hsp70: from cysteine modifications to covalent inhibitors *（Institute of Basic Medicine, Chinese Academy of Medical Science）*	156
10	16:10-16:25	Honghui Zhang	CHK1 Controls Zygote Pronuclear Envelope Breakdown by Regulating F-actin through Interacting with MICAL3 *（Shandong University, China）*	157

S15 亚细胞结构的可视化前沿

Time:4 Dec. 13:30-16:00

No	Time	Speaker	Title / Affiliation	Page
	13:30-16:00	Chairs: Liangyi Chen, Lei Wang		
1	13:30-13:50	Hua Han	扫描电镜三维重建技术在细胞结构分析的应用 *(Institute of Automation, CAS, China)*	158
2	13:50-14:10	Yi Yang	活细胞内RNA的时空分辨追踪 *(East China University of Science and Technology)*	159
3	14:10-14:30	Hanqing Xiong	耦合分子振动光谱的新型活细胞荧光成像技术 *(Peking University)*	160

4	14:30-14:45	Liqing Liu	DeepContact: High throughput quantification of membrane contact site based on electron microscopy imaging *(Institute of Biophysics, CAS, China)*	161
5	14:45-14:55	Shaoling Qi	Seeing Is Solving -- Stunning Details in Living Cells Using Evident SIM-ultimate *(EVIDENT(Shanghai)Co. Ltd)*	162
6	14:55-15:05	Renyao Wang	Leica’s latest advances in CLEM technology *(Leica Microsystems)*	163
7	15:05-15:25	Yongdeng Zhang	单分子定位超分辨成像技术与应用 *（Westlake University, China）*	164
8	15:25-15:45	Yuzheng Zhao	活细胞代谢监测示踪与生命健康 （East China University of Science and Technology）	165
9	15:45-16:00	Bei Liu	Solvatochromic biosensor reveals conformational changes of single molecules in living cells *(Peking University)*	166
16:30-17:30 亚细胞结构与功能分会工作会议				

S9 表型组学与人类健康/Phenomics and Human Health

Time: 4 Dec. 13:30-16:30

No	Time	Speaker	Title / Affiliation	Page
13:30-16:30 Chairs: Tangchun Wu, Mei Tian				
13:30-13:35 Introduction				
1	13:35-14:00	Yuanzeng Min	纳米材料用于药物递送和免疫调节 *（University of Science and Technology of China）*	167
2	14:00-14:25	Daowen Wang	KSHV and dilated Cardiomyopathy *(Huazhong University of Science and Technology, China)*	168
3	14:25-14:50	Huiru Tang	定量代谢组学与精准医学 *(Fudan University, China)*	169
14:50-15:15 Tea Break				
4	15:15-15:40	Chaolong Wang	基于多元孟德尔随机化构建糖脂类性状的因果互作网络 *(Huazhong University of Science and Technology, China, China)*	170
5	15:40-16:05	Chen Ding	蛋白质组技术在临床中的应用 *(Fudan University, China)*	171

6	16:05-16:30	Shaohua Fan	Large-scale genomic data analyses reveal novel loci associated with phenotypic variation and genetic disease in humans *(Fudan University, China)*	172

Closing Ceremony

Time	Schedule
17:00-17:15	Closing Ceremony

Workshop1 Evident显微成像专题报告：更智能，更精准，更灵活

时间：12月3日 11：30-12：40

No	时间	报告人/单位	报告题目
11：30-12：40			
1	11:30-11:50	王咏婕博士Evident 高级工程师	多模态超分辨活细胞成像系统SIM-ultimate
2	11:50-12:05	冯思远 Evident高级工程师	新世代一体化智能成像解决方案APEXVIEW APX100
3	12:05-12:40	Mitsuru Araki *Evdient Deputy General Manager*	液液相分离（LLPS）研究快速精准的光操作解决方案

Workshop 2 HIS-SIM活细胞超分辨显微技术介绍及应用演示

时间：12月4日 11: 30-12：40

No	时间	报告人/单位	报告题目
11: 30-12：40			
1	11：30-11：55	吴梓涵 广州超视计生物科技有限公司	HIS-SIM超分辨技术介绍
2	11：55-12：40	吴梓涵 广州超视计生物科技有限公司	HIS-SIM超分辨应用演示

PL-1/12-3(8:45-9:30）

从口腔走向全身的健康使者-硝酸盐

王松灵

首都医科大学

硝酸盐、亚硝酸盐大多被报道其有害性，尤其是与消化道肿瘤有关，至今大众媒体仍然如此宣传，可谓谈虎色变。本课题组基于唾液中硝酸盐浓度是血液中5-10倍这一生理现象，逻辑推理提出科学问题，围绕硝酸盐、亚硝酸盐的来源，转运机制，生理作用与疾病防治应用及其安全性等关键科学问题进行了20余年系统专题研究。在创建的小型猪腮腺萎缩模型上研究明确腮腺是机体自血中转运硝酸盐至唾液的主要器官。利用唾液腺模式器官研究发现Sialin是哺乳动物细胞膜硝酸盐转运通道，经Sialin转运的硝酸盐在不同细胞内均可转化为一氧化氮（NO），并有相应的较广泛的生理作用，包括增加血流，增强免疫，机体保护等。Sialin在唾液腺、大脑、肝、肾、心血管等组织器官广泛高表达，Sialin介导细胞内多种生物学功能，包括提升线粒体功能、调节细胞增殖及细胞自噬等，硝酸盐和Siali具有维持机体器官、组织、细胞及分子稳态的重要作用，为此提出稳态医学的理念。口服无机硝酸盐具有胃肠及肝脏保护作用，鼻咽癌头颈肿瘤放射治疗保护唾液腺作用，调控机体免疫功能和微生态稳态及在代谢性疾病及老年性疾病等的防治作用。亚硝胺是致癌剂，不应与硝酸盐、亚硝酸盐混为一谈。通过人工智能（AI）技术分析得出硝酸盐的最佳配伍是维生素C药效较单纯无机硝酸盐更高，作用更强，研发了基于硝酸盐+维生素C新药-耐瑞特，具有潜在较广泛的应用前景。

PL-2/12-3(9:30-10:15）

THz与生物物理

刘国治

军事科学院

PL-3/12-3(10:30-11:15)

Mitochondrial surveillance pathway mediates organismal aging

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As the demographics of the population age, the cost of this aged population could be drastic increase. Deciphering the molecular basis of aging and developing drugs for anti-aging treatments to create a healthier older population has become increasingly challenging. Mitochondria are the powerhouse of a cell and serve as central hubs for cellular metabolism, thus it is essential for maintaining mitochondrial homeostasis. Our previous work discovered that mild mitochondrial stress within the nervous system can be sensed and responded to by the distal tissues via a secreted Wnt signal, resulting in lifespan extension in *C. elegans* (*Cell*, 2018; *Cell Reports*, 2022). More importantly, the neuronal mitochondrial stress can also communicate to the germ cells, which promotes the maternal inheritance of elevated levels of mitochondrial DNA (mtDNA), thereby passing down a "stress memory" to offspring, enabling descendants with a greater tolerance to stress and a longer lifespan (*Nature Cell Biology*, 2021). Furthermore, we also revealed that early-life mitochondrial stress communicates with the epigenome via the mitochondrial metabolite to change gene expressions that are beneficial to longevity (*Cell*, 2016; *Science Advances*, 2020). Together, these results open new avenues of research to explore the inter-tissue mitochondrial stress signaling communication during aging in higher model organisms. The understanding of how the mitochondrial surveillance pathways may impinge upon the aging process and physiology will ultimately promote the development of therapeutic targets to promote mitochondrial function and combat age-related neurodegenerative diseases.

S11-1/12-3(13:00-13:30）

铁基纳米酶

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S11-2/12-3(13:30-14:00)

Construction of Bio-inspired Nanozymes and Their Applications

Xiaogang Qu

Changchun Institute of Applied Chemistry , CAS

S11-3/12-3(14:00-14:30)

Self-assembly of porous nanomaterials for enzyme-mimicking catalysis

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Different from the traditional porous catalysts, metal-organic frameworks (MOFs) have been recognized as the most appropriate candidate to mimic enzymes, because their ordered arrangement of metal active centers and organic ligands and tunable geometry of cavities or channels provide the confined environment akin to enzymes. In this report, I will focus on self-assembly of MOFs based nanomaterials as well as their applications in enzyme-mimicking catalysis, which includes the following three parts: (1) Fe-O clusters anchored on nodes of MOFs for direct methane oxidation. The Fe-O clusters are grafted onto Zr_6 nodes of UiO-66, while the organic terephthalic acid (H_2BDC) ligands of UiO-66 are partially substituted with modulators of acetic acid (AC) or trifluoroacetic acid (TFA). The TFA group coordinated with Zr_6 node of UiO-66 enhances the oxidation state of adjacent Fe-O cluster due to its electron-withdrawing ability, promotes the activation of C-H bond of methane and increases its selective conversion, thus leading to the extraordinarily high C1 oxygenate yield compared those modulated with AC. (2) Creating enzyme-mimicking nanopockets in MOFs for catalysis. The enzyme-mimetic nanopockets are fabricated inside the typical UiO-66 by coordinating zirconium nodes with BDC ligands plus modulators including formic acid (FC), AC or TFA. When used in transfer hydrogenation of alkyl levulinates with isopropanol towards gamma-valerolactone (GVL), these modulators endow zirconium sites with enhanced activity and selectivity plus good stability. This improvement mainly originates from the conformational change of modulators in the nanopocket to assist forming the rate-determining six-membered-ring intermediate at zirconium sites. (3) Tunable chiral MOFs toward visible light-driven asymmetric catalysis. The organic ligand integrated with chiral centers is coordinated with different metal ions including Zn^{2+}, Zr^{4+}, and Ti^{4+} to construct chiral MOFs. These MOFs exhibit significantly improved conversion rate and stereoselectivity in asymmetric α-alkylation of aldehydes under visible light. Notably, photocatalytic performance can be tailored by using MOFs with varied metal ions, owing to the tunable electron transfer property between metal ions and chiral ligands. Altogether, MOFs exhibit great potential to mimic enzymes for achieving high catalytic efficiency.

S11-4/12-3(14:30-15:00）

适冷纳米酶

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S11-5/12-3(15:00-15:30)

Tuning Nanozymes at the Atomic Scale for Sensitive Biosensing

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Nanozymes have received great interest and become a rising research area, which have been intensively explored in various fields such as biosensing and biomedical applications. Nanomaterials with abundant atomic composition and complex structural features bring more difficulties in discerning the real active sites and further revealing the structure–activity relationship. Rational synthesis of highly active nanozymes and in-depth understanding of the nature of catalysis at the atomic scale are highly desirable. To further enhance enzyme-like catalytic activities, we focus on the vivid mimicking of natural enzymes and the rational design of nanozymes with superior enzyme-like activities at the atomic scale. Moreover, in-depth understanding of their catalytic nature is expected to provide practical guidance on the design of advanced nanozymes. Taking advantage of their excellent enzyme-like activities and unique physicochemical properties, their applications in biosensing have been explored, achieving the sensitive detection of a series of target molecules.

S11-6/12-3(15:30-16:00)

Nanozymes: from rational design and biomedical applications

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Nanozymes are functional nanomaterials with enzyme-like catalytic activity. They are emerging enzyme mimics and receiving great attention recently. Here we report our efforts in developing design strategies of high performance nanozymes, including using Sabatier principle to design peroxidase mimics and employing data-informed strategy to discover hydrolytic nanozymes. Then we take the therapy of inflammatory bowel disease as an example to show the promise of nanozymes in biomedical applications.

References:

1. J. Wu, et al., *Nanomaterials with enzyme-like characteristics (nanozymes): next-generation artificial enzymes (II)*, **Chemical Society Reviews**, 2019, 48, 1004.
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3. S. Li, et al., *Data-informed discovery of hydrolytic nanozymes*, **Nature Communications**, 2022, 13, 827.
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5. Y. Liu, et al., *Integrated cascade nanozyme catalyzes in vivo ROS scavenging for anti-inflammatory therapy*, **Science Advances**, 2020, 6, abb2695.
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7. Q. Wang, et al., *A Valence-Engineered Self-Cascading Antioxidant Nanozyme for the Therapy of Inflammatory Bowel Disease*, **Angewandte Chemie-International Edition**, 2022, 61, e202201101.

S2-1/12-3(13:00-13:20）

Analysis of intercellular interactions with single-cell secretomic analysis microchip

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S2-2/12-3(13:20-13:40）

Role of the mechanosensing machinery in myogenesis

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Skeletal muscle comprises thousands of multinucleated cells called myofibers, generated by the fusion of myogenic myoblast cells. Myofibers are capable of regenerating themselves in response to the damage caused by repetitive contraction and relaxation. Muscle satellite cells (MuSCs)—stem cells that reside on myofibers—play a fundamental role in the regeneration process; MuSCs appear to be activated by mechanical stresses such as membrane tension, and then to be differentiated into fusogenic myoblast cells. After fusion of myoblasts—either with each other or with injured myofibers—the resultant multinucleated myotubes mature to become functional myofibers. Previous literature has shown that the regeneration process of injured myofibers is impaired in patients with muscle diseases called muscular dystrophy; however, the molecular mechanisms underlying MuSC-dependent regeneration of myofibers and the pathogenesis of muscular dystrophy remain unknown. We previously identified PIEZO1, a mechanosensitive Ca^{2+} channel which is activated by membrane tension, as a key regulator of morphogenesis of myotubes (*Nat.Commun,.*2018). Moreover, after utilizing MuSC-specific *Piezo1*-deficient mice, our results show that PIEZO1 plays a role in regeneration processes such as cell proliferation and migration, suggesting that the mechanosensing machinery is central to myofiber regeneration.

S2-3/12-3(13:40-14:00）

Regulation of unconventional secretion by coronavirus factors

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S2-4/12-3(14:00-14:20）

Liquid phase condensation in living cells

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In recent years, liquid-liquid phase separation has taken the biology world by storm, with this process now thought to drive the formation of dozens of intracellular structures, which represent condensed forms of biomolecular matter. However, we are still largely in the dark about the molecular and biophysical factors that govern where and when these condensates form in living cells and how the spatiotemporal dynamics are linked to their biological functions and diseases.

Here, we combine optogenetic tools and physical theories to show that condensation nucleation occurs through a physical process akin to that in inanimate materials, but the efficacy of nucleation sites can be tuned by their biomolecular features. By quantitatively characterizing the nucleation kinetics of endogenous and biomimetic condensates in living cells, we find that key features of condensate nucleation can be quantitatively understood through classical nucleation theories (CNT). Nucleation rates can be substantially enhanced by compatible biomolecular seeds, and the kinetics of cellular processes can affect condensate nucleation rates and specificity of location. This quantitative framework sheds light on the intracellular nucleation landscape, and opens up the frontiers for engineering synthetic condensates precisely positioned in space and time.

Reference

[1] S. F. Shimobayashi, Pierre Ronceray, David W. Sanders, Mikko P. Haataja, and C. P. Brangwynne*, “Nucleation landscape of biomolecular condensates", *Nature*, 599 (7885), 503-506, (2021).

S2-5/12-3(14:20-14:35）

Imaging method for membrane research

Jianping Xu

Leica Microsystems

Microscopic observation of membrane structure, membrane transport and dynamic tracking have always been used by scientists. In recent years, there are some new imaging techniques for membrane research. Let's give them a brief introduction.

1. Super resolution microscopy for cell membrane
2. FRAP for phase separation
3. FLIM-FRET for membrane tension, pH monitoring.

S2-6/12-3(15:00-15:20）

RAB-8-dependent unconventional protein secretion in *C. elegans*

Xianghong Wang, Xinxin Li, Junkai Wang, Jiabin Wang, Can Hu, Jia Zeng, Anbing Shi, and Long Lin

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Unconventional protein secretion (UPS) pathways are conserved across species. Nevertheless, due to the lack of relevant *in vivo* models, how UPS operates in the polarized cells of living animals remains a challenging problem in the field. Here we recognize SMGL-1/NBAS as a novel apical Golgi-bypassing UPS regulator in the *C. elegans* intestine. SMGL-1 resides in the ER-Golgi intermediate compartment and adjacent RAB-8-positive structures, and NRZ complex component CZW-1/ZW10 is required for this residency. Notably, SMGL-1 acts as a guanine nucleotide exchange factor for RAB-8, ensuring UPS of membrane proteins by driving the activation of RAB-8. However, RABI-8/Rabin8, a putative Rab8GEF, does not possess GEF activity toward RAB-8 *in vivo*. Instead, RAB-11 recruits RABI-8 onto the endosomal compartments, and RABI-8 curbs the GEF efficacy of SMGL-1 by undermining the SMGL-1 oligomerization state, indicating that a tightly controlled RAB-8 activity is required for apical UPS. Furthermore, we show that *Pseudomonas aeruginosa* infection elevated the expression of SMGL-1 and RAB-8. Loss of SMGL-1 or RAB-8 compromised resistance to environmental colchicine, arsenite, and pathogenic bacteria. These results suggest that the SMGL-1/RAB-8-mediated UPS could integrate environmental signals to serve as a host defense response. Together, by establishing the *C. elegans* intestine as a multicellular model, our findings provide insights into RAB-8-dependent Golgi-bypassing UPS, especially in the context of epithelia *in vivo*.

S2-7/12-3(15:20-15:40)

Single-molecule imaging analysis of G protein-coupled receptor signalosome

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G-protein-coupled receptors (GPCRs) are major drug targets that act as a signaling hub via interaction with G proteins and arrestins on the plasma membrane. Biased ligands with pathway-selective activity have attracted much attention as drugs with lower side effects. However, it is yet to be clear how the multiple signaling pathways of GPCR are spatial-temporally regulated in living cell membrane.

Here we show that a co-clustering of GPCRs and signaling molecules in a membrane domain is closely related to their function including G protein binding, GRK-dependent phosphorylation and arrestin/clathrin-dependent endocytosis. First, the single-molecule imaging analysis of various GPCRs demonstrates a general feature that activated GPCRs are entrapped into an immobile membrane domain. Then, we show a novel signalosome that regulates the signal-bias of the angiotensin signaling by AT1R, a class A GPCR. The NanoBiT assays and BRET imaging revealed the AT1R/G protein/GRK preassembly complex in living cell membrane. The dual color single-molecule imaging analysis suggested that the preassembly complex regulates the signal bias in a confined region of the plasma membrane. Finally, we discuss future applications of the next-generation high-content analyzer, which automates the single-molecule imaging analysis, for future pharmacology and drug screening.

S2-8/12-3(15:40-16:00)

Mechanistic Insights into Multiple-step Transport of Mitochondrial ADP/ATP Carrier

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The ADP/ATP carrier (AAC) is crucial for mitochondrial functions by importing ADP and exporting ATP across the inner mitochondrial membrane. However, the mechanism of highly specific ADP recognition and transport by AAC remains largely elusive. In this work, spontaneous ADP binding process to the ground c-state AAC was investigated through rigorous molecular dynamics simulations of over 31 microseconds in total. With improved simulation strategy, we've successfully identified a highly specific ADP binding site in the upper region of the cavity, and this site exhibits selectivity for ADP over ATP based on free-energy calculations. Sequence analyses on adenine nucleotide transporters also suggest that this subgroup uses the upper region of the cavity, rather than the previously proposed central binding site located at the bottom of the cavity to discriminate their substrates. Identification of the new site unveils the unusually high substrate specificity of AAC and explains the dependence of transport on the flexibility between *anti* and *syn* glycosidic conformers of ADP. Moreover, this new site together with the central site supports early biochemical findings. In light of these early findings, our simulations described a multi-step model in which the carrier uses different sites for substrate attraction, recognition and conformational transition. These results provide new insights into the transport mechanism of AAC and other adenine nucleotide transporters.

S3-1/12-3(13:00-13:15)

Beta-arrestin 2 aggravates non-alcoholic steatohepatitis via the metabolic reprogramming of macrophages

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Non-alcoholic fatty liver disease (NAFLD) is a major healthcare burden worldwide. It is consisted of a spectrum of liver disorders ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), cirrhosis and liver cancer. Macrophage-mediated inflammation has been implicated in the pathogenesis of NASH, but the immunometabolic program underlying regulation of macrophage activation remains unclear. Beta-arrestin 2 (Arrb2) is a multifunctional adaptor protein that is highly expressed in human bone marrow tissues and macrophages. However, whether Arrb2 regulates macrophage metabolism and NASH process is not clear. Here, we observed that Arrb2 expression was significantly increased in the hepatic macrophage of NASH patients and HFD-fed mice. Hepatic steatosis, inflammatory responses and fibrosis were ameliorated in Arrb2 global KO mice fed with HFD, MCD or HFHC diet. Arrb2 in macrophages but not hepatocyte contributed to the development of NASH through promoting M1 polarization of macrophages. Mechanism study showed that Arrb2 could act as an adaptor protein and promote ubiquitination of IRG1 to inhibit its protein levels. Deletion of Arrb2 in macrophages increased IRG1 expression and promoted further elevation of itaconate, which results in inhibition of SDH activity, thereby enhancing oxidative phosphorylation (OXPHOS), reducing release of mitochondrial reactive oxygen species (mtROS) and inhibiting Hif-1α/IL-1β axis. Importantly, up-regulation of Arrb2 expression was also observed in circulating monocytes from NASH and NAFL patients compared with those from healthy controls. Arrb2 levels in monocytes correlated positively with serum ALT, AST and the number of circulating monocytes in NAFLD patients. Conclusively, silencing myeloid Arrb2 signaling may result in beneficial effects on treating NAFLD and other aseptic inflammatory disorders.

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S3-2/12-3(13:15-13:30）

Circadian reprogramming of adipose tissue in obesity

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High-fat diet (HFD) feeding rewires circadian rhythms of peripheral organs including the liver and adipose tissue. While the liver has been extensively studied, it remains largely unknown whether and how HFD organizes circadian biology in adipose tissue. Here, we took a systems approach to profile diurnal transcriptome of adipose tissue in diet-induced obese mice either put on low-fat diet (LFD) that reduces weight or still fed HFD. We detected about 200 and 2,500 diurnal genes in HFD and LFD, respectively. Pathway analysis revealed that rhythmic pathways in HFD are represented by circadian rhythm, ribosome biogenesis, nucleosome organization, whereas those in LFD are represented by myeloid cell function. Remarkably, the majority of the circadian clock genes except *Clock* exhibit robust diurnal rhythm in the adipose tissue of HFD-fed mice. We further confirmed the role of the dampened *Clock* rhythm in diet-induced obesity. Together, our work defines the circadian signatures in the adipose tissue of diet-induced obese mice and shed light on potential clock-modulated tissue-specific pathways during obesity.

S3-3/12-3(13:30-13:45）

Metabolic enzymes moonlighting as RNA binding proteins

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RNA Binding proteins (RBPs), involved in regulating aspects of RNA metabolism, have played key roles in our understanding of cellular pathways and their associated diseases. However, the published techniques for proteomic analysis of RBPs have problems of limited scope or insufficient specificity. To improve the RBPs proteomic analysis, we created a new protein (High-Affinity RNA binding Domain protein, HARD) with non-selective, high-affinity binding for RNA by de novo design and utilized HARD protein to achieve affinity purification of covalent RNA-protein complexes. We applied this method to systematically analyze the RBPs proteome of human and mouse. To our surprise, there are 7,000-8,000 proteins with RNA-binding capability in human and mouse, and about 5,000 of which are homologous between human and mouse, providing a good foundation for future research on the function and regulation of RBPs.

S3-4/12-3(13:45-14:00）

Contribution of metabolic alteration by genetic variations to human longevity

Yang Xiang

Nanchang University

S3-5/12-3(14:00-14:15）

Intestine---A new perspective on the regulation of metabolic homeostasis

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Metabolic homeostasis imbalance is the core factor of obesity and its related complications. In recent years, intestine, especially intestinal microorganisms, has been considered as an important regulator of metabolic homeostasis. The dialogue between intestinal microorganisms and adipose tissue regulates the occurrence and development of obesity. We found that adiponectin secreted by adipose tissue can affect insulin sensitivity by regulating the composition and function of intestinal microorganisms. As one of obesity's complications, cardiovascular disease has become the first cause of death in the world. We found that akkermansia muciniphila in the gut can reduce metabolic endotoxemia by repairing the damaged intestinal barrier, thus significantly reducing the formation of atherosclerotic plaque in mice caused by high cholesterol and high fat diet. Metabolic disorders and imbalances not only cause atherosclerosis, but also increase the occurrence of tumors, seriously affecting human survival. The efficacy of anticancer drugs is not completely satisfactory. We found that there were specific intestinal microbial strains in patients with good response to anti-cancer treatment, such as b.ovatus and b.xylanisolvens. The effective anti-cancer effect of these specific intestinal microbial strains was mainly achieved by inducing CXCL9 and IFN gamma. These results suggest that the composition of specific intestinal microorganisms at the beginning of cancer treatment can predict the response of patients to anticancer drugs. The supplementation of specific probiotics can be used as an adjuvant treatment of anti-cancer therapy and achieve better therapeutic effect. In conclusion, the intestinal system, especially the interaction between intestinal microorganisms and the host, is becoming a new perspective for the regulation of metabolic homeostasis. The systematic analysis of its molecular mechanism can provide new drug targets for precision treatment.

S3-6/12-3(14:15-14:30）

细胞空间站-亚细胞结构成像探索

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为了更好地理解代谢过程和疾病发生机理，需要观察线粒体，内质网等细微结构的精确定位和分布，以阐明生物大分子如何组成细胞的基本结构，重要的活性因子如何调节细胞的主要生命活动等。如何打破常规光学显微镜在时空分辨率上的限制，聚焦活体样品，探索生命动态过程？蔡司提供多种研究显微镜解决方案，助力更好的理解诸多细胞生理过程，精细区分超微结构，对快速的动态过程进行捕捉，例如线粒体内外膜结构、细胞内囊泡运输、膜结构等等。

S3-7/12-3(14:30-14:45）

CRL4-COP1: a glucose-sensing E3 in physiology and metabolic diseases

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The Warburg effect, characterized by aerobic glycolysis, provides multiple survival advantages to rapidly proliferating cells including cancer cells. Yet, it remained unclear how such metabolic reprograming is widely achieved amidst tumor heterogeneity. We demonstrate a glucose-dependent proximal signaling axis that reinforces glucose uptake and glycolysis, thus constituting a positive feedback loop that tends to consolidate the Warburg effect. Central to this axis is the identification of CRL4-COP1 as a glucose-sensing E3, whose assembly is strictly induced by glucose, via a post-translational medication cascade. Remarkably, while CRL4-COP1 degrades the obesity-associated transcription factor ETV5 to promote insulin secretion from beta cells, it targets another transcription factor to derepress glucose uptake and glycolysis in cancer cells, suggesting that CRL4-COP1 is a ubiquitous glucose-responsive E3 with spatiotemporal specificity and consequences. That mammalian and plant CRL4-COP1 both respond to their energy source (glucose vs light) underscores evolutionarily conserved roles of CRL4COP1 in energy sensing and utilization processes.

S3-8/12-3(14:45-15:00）

The Polymodal WAT Browning in Metabolism

Junli Liu

Shanghai Sixth People's Hospita

S3-9/12-3(15:00-15:15)

Bone marrow derived-mesenchymal stem cell improves diabetes-associated fatty liver via mitochondria transformation in mice

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Background: Non-alcoholic fatty liver disease (NAFLD) has become a global epidemic disease. Its incidence is associated with type 2 diabetes mellitus (T2DM). Presently, there is no approved pharmacological agents specially developed for NAFLD. One promising disease-modifying strategy is the transplantation of stem cells to promote metabolic regulation and repair of injury.

Method: In this study, a T2DM model was established through 28-week high-fat diet (HFD) feeding resulting in T2DM-associated NAFLD, followed by the injection of bone marrow mesenchymal stem cells (BMSCs). The morphology, function, and transfer of hepatocyte mitochondria were evaluated in both vivo and in vitro.

Results: BMSC implantation resulted in the considerable recovery of increasing weight, HFD-induced steatosis, liver function, and disordered glucose and lipid metabolism. The treatment with BMSC transplantation was accompanied by reduced fat accumulation. Moreover, mitochondrial transfer was observed in both vivo and vitro studies. And the mitochondria-recipient steatotic cells exhibited significantly enhanced OXPHOS activity, ATP production, and mitochondrial membrane potential (MMP), and reduced reactive oxygen species (ROS)levels, which were not achieved by the blocking of mitochondrial transfer.

Conclusion: Mitochondrial transfer from BMSCs is a feasible process to combat NAFLD via rescuing dysfunction mitochondria, and has a promising therapeutic effect on metabolism-related diseases.

Keywords: BMSCs, diabetes, NAFLD, mitochondrial, mitochondrial transfer, metabolism

S14-1/12-3(13:00-13:30）

Single cell atlas of the aging and light/dark-adapted retina

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The human retina is a complex neural tissue that detects light and sends visual information to the brain. However, the molecular and cellular processes that underlie aging primate retina and light/dark-adapted retina remain unclear. Therefore, we used single cell sequencing to dissect the comprehensive transcriptomic atlas of the aging and light/dark-adapted retina. The results indicated that the molecular changes of the aging and light/dark-adapted retina occurred in a region- and cell-type- specific manner. In addition, the retina showed dynamic molecular changes and specifically enriched signaling pathways during aging and light/dark adaptation processes. Importantly, Müller glial cells were identified as a hub cell in the intercellular interactions, displaying complex cell-cell communication with other retinal cells. Together, these datasets are valuable for understanding the molecular characteristics of the functional retina, as well as the molecular regulation of aging progression and related retinal diseases.

S14-2/12-3(13:30-14:00）

TBD

Chen Wu

Peking Union Medical College, China

S14-3/12-3(14:00-14:30）

Spatial-temporal transcriptional landscape of mammalian hypothalamus development

Xin Zhou

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The hypothalamus comprises various nuclei and neuronal subpopulations that control fundamental homeostasis and behaviors. However, spatiotemporal molecular characterization of hypothalamus development in humans is largely unexplored. Here,we revealed spatiotemporal transcriptome profiles and cell-type characteristics of human hypothalamus development and illustrated the molecular diversity of neural progenitors and the cell-fate decision, which is programmed by a combination of transcription factors. Different neuronal and glial fates are sequentially produced and showed spatial developmental asynchrony. Moreover, human hypothalamic gliogenesis occurs at an earlier stage of gestation and displays distinctive transcription profiles compared with those in mouse. Notably, early oligodendrocyte cells in human exhibit different gene patterns and interact with neuronal cells to regulate neuronal maturation by Wnt, Hippo, and integrin signals. Overall, our study provides a comprehensive molecular landscape of human hypothalamus development at early- and mid- embryonic stages and a foundation for understanding its spatial and functional complexity

S14-4/12-3(14:30-15:00）

多维度单细胞分析技术

Jianbin Wang

Tsinghua University, China

S14-5/12-3(15:00-15:30）

Single-cell architecture and functional requirement of lncRNA and alternative splicing during hematopoietic stem cell formation

Jia Yu

Chinese Academy of Medical Sciences

S14-6/12-3(15:30-16:00)

Decoding the molecular mechanisms of ultrasound perception in bat auditory cortex

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Unlike megabats relying on the well-developed vision, microbats utilize ultrasonic echolocation (UE) to navigate and prey. However, how ultrasound is perceived in their auditory cortices (ACs) remains elusive. Here, we generated single-nucleus AC atlas of two UE microbat species (*Rhinolophus sinicus* and *Myotis ricketti*) and two non-UE megabat species (*Rousettus leschenaultii* and *Cynopterus sphinx*) after obtaining their reference-quality genomes. Cross-species comparison revealed significant differences in the inhibitory neurons between UE versus non-UE bats, where parvalbumin (PV)-expressing inhibitory neurons were validated to be crucial for ultrasound perception. Furthermore, we identified an important ultrasound perception related gene by functional and behavioral experiments in mice. Together, our high-quality bat genomes and AC atlases are rich resources for further bat studies, and our findings provide unique insight for understanding the molecular mechanisms of ultrasound perception in mammalian AC.

S5-1/12-3(13:00-13:25)

TMC Proteins Modulate Membrane Excitability through a Background Leak Conductance

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Mutations in transmembrane channel-like (TMC) proteins TMC1 and TMC2 cause deafness and vestibular defects in mammals, however, their precise action modes are elusive. Here, we discover that both TMC-1 and TMC-2 are required for normal egg laying in *C. elegans*. Mutations in these TMC proteins cause membrane hyperpolarization and disrupt the rhythmic calcium activities in both neurons and muscles involved in egg laying. Mechanistically, TMC proteins enhance membrane depolarization through background leak currents and ectopic expression of both *C. elegans* and mammalian TMC proteins results in membrane depolarization. Therefore, we have identified an unexpected role of TMC proteins in modulating membrane excitability. Using genetic screening, we are searching key molecules which aid TMC proteins in “leaking” and in “mechano-sensing”. Our results may provide mechanistic insights into the functions of TMC proteins in hearing loss and other diseases.

S5-2/12-3(13:25-13:50)

人工耳蜗植入的听觉生理基础

Fanglei Ye

The First Affiliated Hospital of Zhengzhou University

S5-3/12-3(13:50-14:15)

TMC1 and TMC2 Proteins Are Pore-Forming Subunits of Mechanosensitive Ion Channels

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Transmembrane channel-like (TMC) 1 and 2 are required for the mechanotransduction of mouse inner ear hair cells and localize to the site of mechanotransduction in mouse hair cell stereocilia. However, it remains unclear whether TMC1 and TMC2 are indeed ion channels and whether they can sense mechanical force directly. Here we express TMC1 from the green sea turtle (CmTMC1) and TMC2 from the budgerigar (MuTMC2) in insect cells, purify and reconstitute the proteins, and show that liposome-reconstituted CmTMC1 and MuTMC2 proteins possess ion channel activity. Furthermore, by applying pressure to proteoliposomes, we demonstrate that both CmTMC1 and MuTMC2 proteins can indeed respond to mechanical stimuli. In addition, CmTMC1 mutants corresponding to human hearing loss mutants exhibit reduced or no ion channel activity. Taken together, our results show that the CmTMC1 and MuTMC2 proteins are poreforming subunits of mechanosensitive ion channels, supporting TMC1 and TMC2 as hair cell transduction channels.

S5-4/12-3(14:15-14:40)

FCHSD2 is required for stereocilia maintenance and hearing

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Stereocilia are F-actin-based protrusions on the apical surface of inner ear hair cells, and are indispensable for hearing and balancing. Stereocilia of each hair cell are organized into rows of increasing heights, forming a staircase-like pattern. The development and maintenance of stereocilia are tightly regulated, and deficits in this process lead to stereocilia disorganization and hearing loss. Previously, we showed that F-BAR protein FCHSD2 is localized along the stereocilia of cochlear hair cells, and could cooperate with CDC42 to regulate F-actin polymerization and cell protrusion formation in cultured COS-7 cells. In the present work, Fchsd2 knockout mice were established to investigate the role of FCHSD2 in hearing. Our data show that stereocilia maintenance is severely affected in cochlear hair cells of Fchsd2 knockout mice, which leads to progressive hearing loss. Moreover, Fchsd2 knockout mice show increased acoustic vulnerability. Noise exposure causes robust stereocilia degeneration as well as enhanced hearing threshold elevation in Fchsd2 knockout mice. Lastly, Fchsd2/Cdc42 double knockout mice show more severe stereocilia deficits and hearing loss, suggesting that FCHSD2 and CDC42 may cooperatively regulate stereocilia maintenance.

Key Words: FCHSD2; CDC42; hair cells; stereocilia; hearing loss

S5-5/12-3(14:40-15:05)

TMC机械转导通道上膜转运的分子机制

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S5-6/12-3(15:05-15:30)

Deciphering auditory function and molecular mechanism through hearing loss gene variants

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Since the completion of the human genome approximately two decades ago, with the whole genome sequencing popularized, the primary bottleneck in human genetics has shifted from the discovery of variants to the associations between genotype and phenotype, and more recently to the causal mechanisms of variants influencing the human biology. Deafness is the most common clinical sensorineural disorder. Genetic factor is one of the most important causes. The identification of the genes underlying hereditary hearing loss and to decipher its mechanism will be important to prevent the recurrence of hearing loss. In the previous study, our group has completed the genetic testing in 24244 cases with hearing loss and 7502 normal hearing adults across mainland China. Based on the sequencing data, we developed a hereditary deafness database and knowledge base, and integrated gene and variant information from databases such as DVD, ClinVar and HGMD, to provide comprehensive knowledge of hearing loss related genes. Recently, we have completed a large cohort CNV and SV analysis based on whole-genome sequencing. Through the analysis of all kinds of variants in the coding and non-coding regions of hearing loss genes, we have further deciphered the functions and molecular mechanisms of hearing loss related genes.

S5-7/12-3(15:30-15:55)

核转录因子FoxG1在老年性聋发生发展中的作用机制研究

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老年性聋又称年龄相关性听力损失（age-related hearing loss），是与年龄相关的听力损失累积的病理生理变化。老年性聋的发病机制复杂,目前尚无特效的治疗方法。核转录因子FoxG1可通过对线粒体能量代谢及合成的调控，在细胞增殖和分化过程中发挥作用。前期研究发现，FoxG1对成年小鼠毛细胞的存活至关重要，因此，我们针对FoxG1在毛细胞老化进程中的作用机制做进一步深入研究。本研究揭示了在听觉系统退行性变过程中，毛细胞可通过激活以FoxG1和自噬信号为主的内在保护机制，促进其在老化进程中的存活能力。本研究有助于老年性聋相关分子机制的阐明，同时也为老年性聋的临床防治提供了新的靶点。

S4-1/12-3(13:00-13:20）

Lighting up the mechanical forces in living cells at the single-molecule level

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Cells are highly dynamic in tissues, and their functions are constantly regulated by various forms of mechanical forces generated by the pushing, pulling and squeezing, both by other cells and the extracellular matrix (ECM). The mechanical forces generated on the receptor molecules in these processes are tiny, in the range of a few pN to tens of pN, but these forces can precisely regulate the signal transduction process in time and space, thereby directly or indirectly controlling a number of biological responses such as cell differentiation, gene expression, and apoptosis. Therefore, characterizing the interaction between mechanical and biochemical signals at the molecular level is an essential part of understanding the mechanism of cellular mechanical signaling. Here, we present a DNA-based nanotechnology that enables real-time imaging of pN-level molecular forces transmitted through membrane receptors in live cells. Using this technique, we reveal previously unseen force-bearing supramolecular structures (i.e. “mechanical hotspots”) that serve as a "mechanical pivot" to stabilize focal adhesion structure and facilitate its maturation.

S4-2/12-3(13:20-13:40）

Mechano-regulated Recognitions of Membrane Receptors for Viral Infection and Immune Defense

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Recognition of membrane receptors precisely controls many essential physiological and pathological processes, including coronavirus host invasion and immune responses against tumor and infection. Complex biomechanical cues exist widely in vivo and inevitably affect membrane receptors' functions. However, how mechanical force couples with receptor structure to dynamically regulate receptor recognition and triggering still remain unclear. In this talk, I will introduce my lab's recent progresses, using multidisciplinary techniques at single-molecule level to reveal: (1) how mechanical force activate SARS-CoV-2 Spike conformational changes to determine viral entry into host; (2) how mechanical force activates T cell receptors' foreign antigen recognition. These works shed lights on designing novel therapeutic antibodies against SARS-Cov-2 infection and on screening tumor neoantigen.

S4-3/12-3(13:40-14:00)

Reading Time and Preference of CpG Binding Proteins Revealed by Single-molecule Profiling

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The TET3 CXXC domain binds to CpG DNA, serving a basic epigenetic information reading mechanism. During the selective recognition of a CpG motif by a CXXC domain from crowded binding sites in a gene sequence, the protein-DNA interactions are under a complex nonequilibrium state. However, the selective binding dynamics of CpG recognition by epigenetic enzymes in a gene background have been rarely exploited. Here, we used single-molecule magnetic tweezers to quantitatively examine the dynamics of TET3's CXXC domain on a Hoxa9 promoter DNA. Our single-molecule binding profile revealed that CXXC-DNA interactions involve both CpG motifs and their flanking sequences. The binding probabilities of TET3 CXXC in the first CGI of Hoxa9 gene show significant differences for the 20 CpG motifs. Moreover, the residence time of TET3 CXXC differs by about 1000 times in the five distinguished CpG clusters of the Hoxa9 CGI. Finally, we performed multi-state hidden Markov modeling analysis on the zipping/unzipping dynamics of a CpG hairpin, discovering TET3 CXXC's preference on CpG motifs regarding the -2 to +2 flanking bases. Our results shed light on the selective binding dynamics of a CXXC on a gene sequence. This work also benefits studies on protein-nucleic acid interactions in general.

S4-4/12-3(14:00-14:20)

Biomimetic nanopore and its applications in sequencing, structural profiling and single molecule chemistry

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Fast development of nanopore sequencing techniques has re-defined personalized medicine and precision medicine. The commercialized available MinION sequencer, which is nanopore based, has realized direct DNA and RNA sequencing in a palm-sized device. It has a high resolution and can directly identify epigenetic modifications. Mycobacterium smegmatis porin A (MspA) is a critical nanopore sensor that has demonstrated the first nanopore sequencing applications. Its wide vestibule lumen also permits trapping of large biomolecules including DNA aptamers or DNA origamis in a sensing mode defined as nanopore trapping. In specific applications scenarios, it can also directly observe allosteric transition of a single protein. Specially engineered MspA can also clearly monitor single molecule chemical reaction. Its much better performance in single molecule chemistry observation results from a more advantageous conical lumen geometry than an alpha-hemolysin nanopore. With MspA, direct observation of chemical binding of monatomic ions or small molecules were clearly observed. To further boost its application scenarios, a new technique defined as Programmable Nano-Reactor for Stochastic Sensing (PNRSS) was invented. With PNRSS, more than 20 types of single molecule reactions have been successfully monitored. However, the challenge of pore engineering has been omitted.

S4-5/12-3(14:20-14:40）

Dam-methylation of DNA promotes both RecA assembly and homologous DNA pairing revealed by single-molecule experiments

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DNA methylation and homologous recombination are extensively studied in prokaryotes and eukaryotes. Whether DNA methylation directly affects homologous recombination, however, re-mains unexplored. Here, mainly by single-molecule experiments, we report that Escherichia coli RecA (EcRecA) assembles faster and more on Dam-methylated single-stranded DNA (ssDNA), which can be partially explained by that adenine methylation decreases the net negative charge of ssDNA, thus promoting RecA nucleation on ssDNA. EcRecA-ssDNA filaments pair faster with Dam-methylated and hemi-Dam-methylated homologous double-stranded DNA (dsDNA), which can be explained by that m6A enhances the stretchability of dsDNA. Additional single-molecule experiments show that the preference of RecA for Dam-methylated DNA is maintained over distant species including two bacteria Klebsiella pneumoniae, Bacillus subtilis and a flowering plant Arabidopsis thaliana. Based on these findings, we propose that Dam-methylation of DNA directly promotes both RecA assembly on ssDNA and RecA-mediated homologous DNA pairing.

S4-6/12-3(14:40-15:00)

Regulatory mechanisms of mechanical anisotropy and conformational dynamics of flaviviral xrRNAs by single-molecule techniques

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Exoribonuclease-resistant RNAs (xrRNAs) are a group of RNA elements capable of resisting the degradation by exoribonuclease. Flaviviral xrRNAs adopt an unusual ring-like 3D structure centered on a three-way junction which is further stabilized by key tertiary interaction motifs including a three-way junction formed by P1, P2 and P3 and an additional P4 helix, two interwoven pseudoknots (PK1, PK2) and other long-range tertiary interactions, such as complex base-stacking arrangements and base triples. Notably, the PK1 length remains almost identical (1 – 2 bp) but the PK2 length varies from 2 bp to 7 bp across different MBFVs.

A "molecular brace" model has been proposed for xrRNAs to elucidate their high resistance to directional degradation by the 5'→3' exonucleases, but readiness to be traversed by the viral RNA-dependent RNA polymerase (RdRP) approaching in the 3'→5' direction. The xrRNAs are expected to exhibit significant mechanical anisotropy, which however has not been experimentally proved before. By using single-molecule nanopore sensing technique, we explore the mechanisms of directional mechanical stability of the ZIKA virus (ZIKV) xrRNA1. We reveal extreme mechanical anisotropy in ZIKV xrRNA1 which highly depends on Mg^{2+} and the key tertiary interactions. The absence of Mg^{2+} and disruption of the key tertiary interactions strongly affect the structural integrity and attenuate mechanical anisotropy. The significance of ring structure in RNA mechanical anisotropy is further supported by steered molecular dynamics simulations in combination with force distribution analysis. We anticipate the ring structures can be used as key elements to build RNA-based nanostructures for biomaterial and biomedical applications.

To understand how RNA dynamics is regulated and connected to its function, we investigate the folding, conformational dynamics and robustness of Xrn1 resistance of a set of flaviviral xrRNAs using SAXS, smFRET and *in vitro* enzymatic assay. We find that xrRNAs' folding, conformational dynamics and robustness of Xrn1 resistance are strongly correlated and highly Mg^{2+}-dependent, furthermore, the Mg^{2+}-dependence is modulated by PK2 length variations. xrRNA with long PK2 requires less Mg^{2+} to stabilize its folding, exhibits reduced conformational dynamics and strong robustness of Xrn1 resistance at even low Mg^{2+}, and tolerates mutations at key tertiary motifs at high Mg^{2+}, which generally are destructive to xrRNA with short PK2, through enhanced sampling of the native state in the structural ensemble. These results demonstrate an unusual regulatory mechanism of RNA dynamics providing insights into the functions and future applications of xrRNAs.

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S4-7/12-3(15:00-15:10）

NUT中线癌中BRD4-NUT和p300结合在染色质上异常调控基因转录的结构机制

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NUT中线癌是一种罕见的高侵袭性癌症，通常发病于人体的中线部位器官中。NUT癌的致病驱动是由于NUT基因染色体易位，产生了BRD4-NUT融合蛋白并结合到乙酰化染色质上。BRD4-NUT通过招募组蛋白乙酰转移酶（HAT）p300，增加p300的催化活性，高度地乙酰化组蛋白赖氨酸，并促进染色质中的核浓缩，在抗分化基因的异常转录中发挥作用。然而，BRD4-NUT如何招募和激活p300的分子结构机制尚不清楚。本报告发现，BRD4-NUT融合蛋白的NUT蛋白区域中包含两个与p300中的TAZ2结构域相结合的反式激活结构域（TAD）。通过核磁共振（NMR）结构解析结果表明，这两个结构域（TAD1、TAD2）与四螺旋束的TAZ2结构域结合时，均能形成稳定α-螺旋折叠结构。在体外实验中，NUT蛋白质能凝聚成液态液滴，通过1:2化学计量比滴加TAZ2蛋白质促进了液滴增强。BRD4-NUT/p300中的TAD/TAZ2双重结合，引发了p300蛋白变构激活以及乙酰化所介导的细胞核染色质上的液态凝聚点，其中富集了组蛋白H3赖氨酸27乙酰化（H3K27ac）和转录调控相关蛋白BRD4L/S、CDK9、MED1和RNA聚合酶II等。ALX1是NUT癌中高表达的癌基因，导致ALX1/Snail信号传导增强和上皮-间充质转化，本研究阐明BRD4-NUT/p300染色质凝聚是激活ALX1基因转录的关键。本报告创新性地揭示：BRD4-NUT在NUT癌中的通过双重结合p300，招募并在染色质上激活p300，用于扩增组蛋白超级乙酰化水平和染色质的液态浓缩，形成了一种前馈式循环，以维持异常的抗分化基因转录和肿瘤细胞增殖的重要结构机制。

S4-8/12-3(15:40-16:00)

Hsp70 Chaperone Machinery in Action

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Hsp70 chaperone machinery is a central hub of the chaperone network. Key to the safeguard function of this machinery is the synergistic cooperation between Hsp40 and Hsp70 on numerous substrates processing. We used NMR spectroscopy in combination with other biophysical tools to determine the solution structures and dynamic features of both Hsp40 in complex with an unfolded client protein and full length Hsp40 with Hsp70. Atomic structures of the various binding sites in the client complexed to the binding domains of the Hsp40 reveal the recognition pattern. Hsp40 engages the client in a highly dynamic fashion using a multivalent binding mechanism that alters the folding properties of the client. Hsp70 binding to Hsp40 displaces the unfolded client and forms a hetero-tetramer. This special architecture of Hsp40-Hsp70 chaperone machinery alters the folding energy landscape and accelerates client folding. Our results also highlight the importance of concerted dynamic engagement between chaperone and clients.

S4-9/12-3(16:00-16:20）

RNA的固体核磁共振研究新方法

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S4-10/12-3(16:20-16:40)

The amyloid structures in cell necroptosis

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Amyloid complexes play the crucial roles in execution of necroptosis and in response to immune defense in both human and mouse. We have structurally characterized the human and mouse RIPK3 homogeneous self-assembly using solid-state NMR, illustrating a well-ordered N-shaped amyloid core structure featured with 3 parallel in-register β-sheets. The structure revealed by solid-state NMR is different from previously published human RIPK1/RIPK3 hetero-amyloid complex which adopts a serpentine fold. Our studies provide a first step to understand how the mouse RIPK1 fibril structural transform to RIPK3 fibril through a RIPK1-RIPK3 hetero-amyloid intermediate. Furthermore, the amyloid formed by mouse RIPK1, human DAI involved in necroptosis were also investigated, revealing interesting findings.

S4-11/12-3(16:40-17:00)

The fluoride permeation mechanism of the fluc channel revealed by solid-state NMR

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Membrane proteins carry out a variety of functions vital to the survival of organisms, such as transport of metabolites and transduction of chemical signals. Understanding the dynamics of these medically important membrane proteins in their native environment is essential to understanding their cellular function. Compared to other techniques, solid-state NMR (ssNMR) spectroscopy can provide atomically detailed and biologically authentic information about membrane protein structure and dynamics. Here, we present our current ssNMR study on the fluorine channel CrcB in liposomes. New fluoride binding sites that were not identified in previous structural studies were observed in the vestibule by combining site-specific ^{19}F labelling and ^{19}F-detected ssNMR methods. One of the two sites in the fluoride permeation pathway was identified as the H_2O molecule by ^{1}H-detected ssNMR. We propose a knock-on permeation model in which fluoride ions are separated by water molecules. Meanwhile, a dynamic hotspot at the loop 1 was observed by comparing the spectra of wildtype CrcB in variant buffer conditions or with its mutants, indicating that this region is important for gating. These results not only provide valuable insights into the permeation mechanism of CrcB, but also have important implications for our deeper understanding of fluoride channels.

S4-12/12-3(17:00-17:20)

In-Situ High-Resolution Measurements on Biomacromolecules

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The question how does the intracellular environment affect the structure, dynamics and stability of a protein and protein-protein interactions has been a centre of interest in the context of understanding proteins function in their native environment. We addressed this question by combining EPR and NMR via site-specific tagging of proteins with paramagnetic tags to elucidate the high-precision conformational space and the stability of biomacromolecules. Pulsed dipolar EPR spectroscopy (PDS) is an ensemble measurement technique that provides unique distance distribution information, typically in the range between 15 and 160 Å. The SDSL/PDS approach primarily detects the introduced spin labels and probes biomacromolecules' structural features in the cell with minimal background signals. In our study, biocompatible spin labels have been introduced and their utility has been demonstrated on challenging adaptations: the resistance of spin-label system to the reducing cellular environment, the efficient and innoxious delivery methods of the labeled biomacromolecules into the cells, and the measurement sensitivity to come close to physiological concentration. We also explored PDS to obtain information on e.g., the disorder of biomacromolecule systems, conformational changes in proteins, and the time scale of the conformational change, in human cells as compared to in buffer solution and cell lysates. Our results highlight the potential of PDS for in-situ study of biomacromolecules as well as the complexities of the effects of the cellular milieu on biomacromolecule structures and stability.

S4-13/12-3(17:20-17:30)

Nucleic acids structural dynamics and interactions with small ligands analyzed by single-molecule magnetic tweezers

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The structural dynamics of nucleic acids secondary structures such as G-quadruplexes (G4s) play an essential role in biological processes. However, determine the nucleic acids folding/unfolding dynamics remains challenging due to the co-existence of multiple structures in a heterogeneous sample. By developing single-molecule magnetic tweezers methods, we systematically analyzed the folding/unfolding kinetics of G-quadruplexes at physiologically relevant solutions and showed that the slow unfolding rate of ~10^{-6} s^{-1} is prevalent in oncogene promoter G-quadruplexes. We identified the major intermediates of G4s with a bulge and provided a new strategy to target the bulged G4s by selectively stabilizing the folding intermediates to modulate their functions. Furthermore, we utilized the single-molecule methods to discovery novel anti-cancer drugs that affecting nucleic acids structural dynamics.

Key word: Single-molecule manipulation ; Folding/unfolding kinetics ; G-quadruplexes; Magnetic Tweezers;

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S4-14/12-3(17:30-17:40）

单分子力谱和分子模拟揭示新冠病毒N501Y突变提高病毒与受体间相互作用力及其分子机制

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蛋白质分子的聚合和特异性固定在其研究和应用中发挥着重要作用，例如蛋白检测、抗体偶联药物构建和单分子研究。通过结合蛋白酶联和点击化学反应，我们发展了一种高效稳定的蛋白固定和聚合方法，大幅提高了单分子实验的效率和精确度［1-2]。我们将该方法应用于新冠病毒突变体黏附机制的研究中，利用力谱精准测量了不同突变株表面刺突蛋白(Spike Protein)中受体结合域（RBD）与对应的人受体蛋白ACE2的相互作用强度，并结合分子动力学模拟在原子水平进行分析和验证[3]。研究结果发现RBD上的N501Y氨基酸突变是导致这些变异株能更强结合ACE2的重要原因之一，显著提高了病毒黏附细胞的强度和概率。该研究为更好的理解和监控新冠病毒以及设计相关中和抗体提供了重要的分子信息，也是首个揭示N501Y这一重要新冠突变后果的实验工作之一，作为重要参考文献之一被世卫组织(WHO)2021年8月新冠突变监控报告引用，也被国家自然科学基金委网站所介绍。

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S1-1-1/12-3(16:30-16:50)

Molecular basis of receptor binding and antibody neutralization of Omicron

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The SARS-CoV-2 Omicron variant exhibits striking immune evasion and is spreading rapidly worldwide. Understanding the structural basis of the high transmissibility and enhanced immune evasion of Omicron is of high importance. Here, using cryo-electron microscopy, we present both the closed and the open states of the Omicron spike (S) protein, which appear more compact than the counterparts of the G614 strain, potentially related to enhanced inter-protomer and S1–S2 interactions induced by Omicron residue substitution. The closed state showing dominant population may indicate a conformational masking mechanism for the immune evasion of Omicron. Moreover, we captured three states for the Omicron S–ACE2 complex, revealing that the substitutions on the Omicron RBM result in new salt bridges and hydrogen bonds, more favourable electrostatic surface properties, and an overall strengthened S–ACE2 interaction, in line with the observed higher ACE2 affinity of Omicron S than of G614. Furthermore, we determined the structures of Omicron S in complex with the Fab of S3H3, an antibody that is able to cross-neutralize major variants of concern including Omicron, elucidating the structural basis for S3H3-mediated broad-spectrum neutralization. Our findings shed light on the receptor engagement and antibody neutralization or evasion of Omicron and may also inform the design of broadly effective vaccines against SARS-CoV-2.

S1-1-2/12-3(16:50-17:10）

基于统计能量以及深度学习的蛋白质设计

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报告简介：蛋白质序列-结构-功能的关系是生命科学的基础问题，同时与应用密切相关。蛋白质设计要回答的是：我们怎样从头设计人工氨基酸序列，让它们也象天然蛋白一样，能自发折叠成确定的、符合预设目标的三维结构和功能？我将介绍用计算机进行蛋白质设计的基本原理，着重报告基于统计能量的主链结构设计模型（SCUBA）、氨基酸序列设计模型（ABACUS）和深度学习的氨基酸序列设计模型ABACUS-R的方法原理和相关的实验验证结果，并分享讨论关于数据和AI驱动的蛋白质计算一些展望和思考。

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S1-1-3/12-3(17:10-17:30)

Structural insights into ATP-dependent processing of long double-stranded RNAs by Drosophila Dicer-2/Loqs-PD complex

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S1-1-4/12-3(17:30-17:50)

NMDA receptors: from atomic structures to diverse physiological functions

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N-methyl-D-aspartate (NMDA) receptors are glutamate-gated and calcium-permeable ion channels that play critical roles in neuronal development and brain function. Dysfunction of NMDA receptors has been implicated in a series of neuropsychiatric diseases, including depression, epilepsy, chronic pain, Alzheimer's disease and autoimmune encephalitis. Functional NMDA receptors are typically assembled as di-heteromeric or tri-heteromeric tetramers with two obligatory GluN1 subunits and two identical or different GluN2 (2A-2D) and GluN3 (3A and 3B) subunits. Formation of such heteromers by seven subunits provides NMDA receptors with a wealth of structural and functional diversity in the brain. By integrating the cutting-edge techniques in single-particle cryo-electron microscopy, electrophysiology, molecular dynamics simulation and artificial intelligence-based drug design, we aim to decode the biophysical and functional diversity of various NMDA receptor subtypes from multi-dimensional levels including atomic structure, gating mechanism, pharmacological and physiological properties. In this presentation, I will talk about 1) Distinct structure and gating mechanism in GluN2C- and GluN2D-incorporated NMDA receptors (unpublished); 2) Molecular mechanism of the rapid-antidepressant ketamine; 3) Structural basis of anti-NMDA receptor autoimmune encephalitis.

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S1-1-5/12-3(17:50-18:05）

The Recent Advances and Application in Cryo-EM

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Since the Nobel Prize in Chemistry in 2017, Cryo-Electron Microscopy (Cryo-EM) has helped scientists solve many life science problems and is playing a more and more important role in many fields such as biomedicine, drug discovery and development, and vaccine design. With advances in Cryo-EM hardware, software, data processing algorithms, and sample preparation techniques, more and more high-resolution protein structures have been resolved with Cryo-EM single particle analysis, thereby deepening our understanding of many life science problems and accelerating structure-based drug design. At the same time, using Cryo-Electron Tomography, scientists can study the in-situ structure and function of proteins and organelles in cells or tissues. This report will introduce the latest Cryo-EM progress and application stories.

S1-1-6/12-3(18:00-18:15）

Structural mechanism of GTP initiating microtubule assembly

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S1-1-7/12-3(18:15-18:30)

Structure and mechanism of NALCN channel complex

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NALCN channel mediates sodium leak currents, which positively tune the resting membrane potential and excitability of the neuron. NALCN and its auxiliary subunits FAM155A, UNC79, and UNC80 co-assemble into a large heterotetrameric channel complex. Genetic mutations of NALCN channel components lead to a spectrum of neurodevelopmental diseases. However, the structure and mechanism of the intact channel complex remain elusive. Here, we present the cryo-EM structure of the mammalian NALCN-FAM155A-UNC79-UNC80 quaternary complex. The structure shows that UNC79-UNC80 form a large piler-shaped heterodimer which was tethered to the intracellular side of the NALCN channel through tripartite interactions with the cytoplasmic loops of NALCN. Two interactions are essential for proper cell surface localization of NALCN. The other interaction relieves the self-inhibition of NALCN by pulling the auto-inhibitory CTD Interacting Helix (CIH) out of its binding site. Our results uncover the structural mechanism of NALCN modulation by UNC79 and UNC80.

S1-1-8/12-3(18:30-18:45）

Computational methods to regulate RNA functions

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Non-coding RNA molecules play essential roles by interacting with other molecules to perform various biological functions. However, it is challenging to determine RNA structures due to their flexibility. Currently, the number of experimentally solved RNA and RNA complex structures is still insufficient. Therefore, computational methods are required to determine the RNA pockets and binding sites to regulate RNA functions. Here, we present the RNA pocket topology resources and the network-based pocket prediction approach for identifying the allosteric druggable pockets with case studies.

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S1-1-9/12-3(18:45-19: 00）

DeepETPicker: Fast and accurate 3D particle picking for cryo-electron tomography using weakly supervised deep learning

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Picking particles of biological macromolecules from their cryo-electron tomography (Cryo-ET) images, often called tomograms, is a critical step in solving their 3D structures in their native environment. Many thousands of 3D particles usually must be picked under very low signal-to-noise ratios. Currently, throughput of automated particle picking methods is limited by their need of a large number of manually annotated particles for training and their high computational cost for particle localization and classification. To overcome these limitations, we have developed DeepETPicker, a deep learning-based method that rapidly and accurately picks 3D particles in tomograms with high reliability. Its training requires only weak labels so that the cost of annotation is substantially reduced. It achieves fast speed in particle localization by using a lightweight architecture and GPU-accelerated pooling operations. Its performance on small macromolecules and in edge voxels is enhanced by using custom architecture design and overlapping tomogram partitions, respectively. When tested on simulated and real tomograms from three datasets, DeepETPicker outperforms competing state-of-the-art methods by achieving the highest speed and accuracy and matches manual particle picking by experts in the resulting structural resolution. It is provided as open-source software with a friendly user interface to facilitate DNN model training and particle picking in crowded intracellular environment.

S1-1-10/12-3(19:00-19:15)

Near-atomic structure of the inner ring of the Saccharomyces cerevisiae nuclear pore complex

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Nuclear pore complexes (NPCs) mediate bidirectional nucleocytoplasmic transport of substances in eukaryotic cells. However, the accurate molecular arrangement of NPCs remains enigmatic owing to their huge size and highly dynamic nature. Here we determined the structure of the asymmetric unit of the inner ring (IR monomer) at 3.73 Å resolution by single-particle cryo-electron microscopy, and created an atomic model of the intact IR consisting of 192 copies from 8 subunits. In each IR monomer, two approximately parallel rhomboidal structures of the inner and outer layers are sandwiched with the Z-shaped Nup188-Nup192 middle layer and Nup188, Nup192 and Nic96 link all subunits to constitute a relatively stable IR monomer, while the intact IR is assembled by loose and instable interactions between IR monomer. These structures reveal various interaction modes and extensive flexible connections in the assembly, providing a structural basis for the stability and malleability of IR.

S8-1-1/12-3(16:30-16:45）

Brain development and neural stem cell mechanism study

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The mammalian brain contains millions of neurons and glial cells. Normal cerebral brain development plays an important role in controlling behavior, learning and cognition. During neurogenesis, neural progenitor cells (NPCs) proliferate and differentiate into neurons of cortical layers, which are precisely controlled by various intracellular and extracellular signaling pathways. NPCs of the brain are mainly PAX6-positive apical progenitor cells and TBR2-positive basal progenitor cells. Although more and more molecules are reported involved in the proliferation of progenitor cells, how neurogenesis is regulated by epigenetic factors during the embryonic development of the cerebral cortex remains largely to be investigated. Here, we found a series of epigenetic molecules and modifications are essential for the proliferation and self-renewal of neural stem cells.

Keywords: Neural development; neural stem cell; neurogenesis

S8-1-2/12-3(16:45-17:00)

线粒溶酶体（mitolysosome）胞吐：帕金森症线粒体质量控制新途径

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Mitochondrial quality control plays an important role in maintaining mitochondrial homeostasis and function. Disruption of mitochondrial quality control degrades brain function. We found that flunarizine (FNZ), a drug whose chronic use causes parkinsonism, led to a parkinsonism-like motor dysfunction in mice. FNZ induced mitochondrial dysfunction and decreased mitochondrial mass specifically in brain. FNZ decreased mitochondrial content in both neurons and astrocytes, without affecting the number of nigral dopaminergic neurons. In human neural progenitor cells, FNZ also induced mitochondrial depletion. Mechanistically, independent of ATG5- or RAB9-mediated mitophagy, mitochondria were engulfed by lysosomes, followed by a vesicle-associated membrane protein 2– and syntaxin-4–dependent extracellular secretion. A genome-wide CRISPR knockout screen identified genes required for FNZ-induced mitochondrial elimination. These results reveal not only a novel lysosome-associated exocytosis process of mitochondrial quality control that may participate in the FNZ-induced parkinsonism but also a drug based method for generating mitochondria-depleted mammal cells.

S8-1-3/12-3(17:00-17:15）

建立神经干细胞移植和人工耳蜗植入相结合的新综合技术体系的研究
The potential application of Stem Cell transplantation in the Cochlear Implants

柴人杰

东南大学

听力障碍是一种常见的耳科疾病。根据WHO统计2005年全球听力障碍人数为2.78亿，占全球人口的4.6%。2006年我国国家统计局公布的调查数据显示，全国耳聋人数为2780万，占全部残疾人总数的四分之一，居残疾人总数第二位。耳聋已成为影响社会政治和经济的全球性健康问题，耳蜗毛细胞和螺旋神经元的不可逆损伤是造成感音神经性聋的核心原因，成年哺乳动物的耳蜗毛细胞和螺旋神经元细胞在受损缺失后不能自发再生从而恢复正常的功能。目前临床上常用的人工耳蜗植入是目前临床应用最广、最有效的现代康复技术之一。人工耳蜗是一种为重度、极重度、甚至全聋的成人及小儿恢复或获得听力的一种电子装置，该装置能把声音信号转变为电信号直接刺激螺旋神经细胞及听神经纤维，可以不依赖毛细胞产生听觉。作为唯一能使全聋病人恢复听觉言语交流能力的医学装置，自从八十年代中期美国FDA批准首例人工耳蜗植入之后，目前全球超过30万患者接受了人工耳蜗移植手术。但人工耳蜗能否产生令患者满意的言语分辨能力完全依赖于残存的螺旋神经元，功能性螺旋神经元数量不足是影响人工耳蜗植入效果的重大医学难题。因此，如何使螺旋神经元在损伤和丢失后修复和再生，是近年来听觉领域研究的重点，而以干细胞为核心的再生医学为我们提供了一个充满希望的解决方案。石墨烯被证明可以作为一种良好的神经界面材料，能显著促进神经干细胞再生神经元，促进新生神经元神经突的生长以及功能成熟。同时石墨烯具有良好的导电特性，而电刺激对以电生理活动为特征的螺旋神经元的发育成熟也是必须的，因此通过石墨烯做为支架能显著促进神经干细胞分化为螺旋神经元。我们课题组和南京鼓楼医院耳鼻喉科主任高下教授合作，利用具有良好神经界面效应和导电特性的纳米材料石墨烯做为神经干细胞移植的支架，结合人工耳蜗的电刺激来显著促进螺旋神经元的再生和功能的成熟；进而建立把神经干细胞治疗和人工耳蜗植入有机结合的新临床综合技术体系，为优化人工耳蜗植入患者听觉言语功能康复奠定理论和实验基础。

S8-1-4/12-3(17:15-17:30)

Discovery of a molecular glue that enhances UPR^{mt} to restore proteostasis via TRKA-GRB2-EVI1-CRLS1 axis

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† These authors share joint first authorship Running title: Ginsenoside Rg3 reverses Parkinson's disease model by enhancing mitochondrial UPR

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Lowering proteotoxicity is a potentially powerful approach for the treatment of neurological disorders, such as Parkinson's disease. The unfolded protein response (UPR) is a major mechanism that preserves the network maintaining cellular proteostasis. In the present study, we developed the screening strategy to discover compounds that significantly enhanced the activation of mitochondrial UPR (UPR^{mt}) through increasing cardiolipin content. We identified that ginsenoside Rg3 (Rg3) increased cardiolipin depending on cardiolipin synthase 1 (CRLS1) in both worms and in human neural cells. Using LiP-SMap (limited proteolysis-mass spectrometry) strategy, we identified GRB2 (growth factor receptor bound protein 2) as a direct target of Rg3 in human neural cells. Rg3 enhances the binding between GRB2 and TRKA (tropomyosin-related kinase A), that transduces signals *via* phosphrorylation of ERK (extracellular signal-regulated kinase). We provided bioinformatic and experimental evidences showing that EVI1 (ecotropic virus integration site-1), the critical oncogenic transcriptional regulator in leukemia, binds to *CRLS1* promoter region and stimulated *CRLS1* expression and subsequently increased cardiolipin content in the presence of Rg3. Rg3 stimulates alpha-synuclein clearance by promoting mitochondrial peripheral fission and mitophagy. In two Parkinson's disease mouse models, Rg3 restores motor function by protecting nigral dopaminergic neurons dependent on GRB2. Consistently, Rg3 protected iPSC-derived dopaminergic neurons by restoring ERK/CRLS1 signaling and mitochondrial function. Our data recapitulate the TRKA-GRB2-EVI1-CRLS1 axis in maintaining proteostasis in Parkinson's disease *via* restoring mitochondrial homeostasis.

Keywords: Parkinson's disease; cardiolipin; UPR^{mt}; Ginsenoside Rg3; GRB2; TRKA; EVI1

S8-1-5/12-3(17:30-17:45)

GFAP hyper-palmitoylation exacerbates neurodegenerative pathology and potential interventions

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The homeostasis of protein palmitoylation and depalmitoylation is essential for proper physiological functions in various tissues, in particular, the central nervous system (CNS). The dysfunction of PPT1 (PPT1-KI, INCL mouse model), which catalyze the depalmitoylation process, results in serious neurodegeneration accompanied by severe astrogliosis in the brain. Endeavoring to determine critical factors that might account for the pathogenesis in CNS by palm-proteomics, GFAP was spotted, indicating that GFAP is probably palmitoylated. Questions concerning if GFAP is indeed palmitoylated in vivo and how palmitoylation of GFAP might participate in neural pathology remain unexplored and are awaited to be investigated. Here we showed that GFAP is readily palmitoylated in vitro and in vivo, specifically, cysteine-291 is the unique palmitoylated residue in GFAP. Interestingly, it was found that palmitoylated GFAP promotes astrocyte proliferation in vitro. Further, we showed that PPT1 depalmitoylates GFAP, and the level of palmitoylated GFAP is overwhelmingly upregulated in PPT1-KI mice, which lead us to speculate that the elevated level of palmitoylated GFAP might accelerate astrocyte proliferation in vivo and ultimately led to astrogliosis in INCL. Indeed, blocking palmitoylation by mutating cysteine-291 into alanine in GFAP attenuate astrogliosis, and remarkably, the concurrent neurodegenerative pathology in PPT1-KI mice. Together, these findings demonstrated that hyper-palmitoylated GFAP plays critical roles in regulating the pathogenesis of astrogliosis and neurodegeneration in CNS, and most importantly, pinpointing that cysteine-291 in GFAP might be a valuable pharmaceutical target for treating INC, and accordingly, the approach of structural based drug design is carrying out to test the treating effect of these potential interventions in INCL mouse model.

Keywords: GFAP; Protein palmitoylation; PPT1; Astrogliosis; Neurodegeneration; Interventions;

S8-1-6/12-3(17:45-18:00）

阿尔茨海默症的表观遗传调控

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阿尔茨海默病（Alzheimer’s disease, 简称AD），是一种常见的衰老相关的神经退行性疾病。衰老是神经退行性疾病的重要风险因素。载脂蛋白E(ApoE)是大脑内丰度最高的载脂蛋白之一，同时也是迟发性阿尔茨海默病的最大风险因素，但是致病机制一直不清楚。我们最近的工作揭示了ApoE对神经元的胆固醇代谢进行重编程的机制，以及这种代谢调控对神经元功能特别是学习记忆过程的影响，同时也揭示了ApoE4导致阿尔茨海默病的全新机制。该研究首先发现了胶质细胞来源的ApoE显著抑制神经元内的胆固醇合成途径上关键酶，从而对神经元的胆固醇合成代谢进行抑制。ApoE通过抑制胆固醇的合成显著累积了胆固醇合成的前体乙酰辅酶A，并显著增加组蛋白的乙酰化水平。该研究表明，ApoE通过调控乙酰化组蛋白在启动子区的水平，调控早期应答基因的转录。进一步的研究发现ApoE对神经元的代谢调控是依赖于其所携带的miRNA来实现的。重要的是，ApoE介导的神经元的代谢和表观遗传调控表现为明显的亚型特异性，ApoE4调控神经元胆固醇代谢和表观遗传的能力显著弱于ApoE3。这些结果揭示了ApoE4是通过对神经元代谢和表观遗传的调控参与阿尔茨海默病的病理进程。

S8-1-7/12-3(18:00-18:15）

The structure and function of ALS-linked C9orf72 complex

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A massive intronic hexanucleotide repeat (GGGGCC) expansion in C9orf72 is a genetic origin of familial amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Studies have found that this repeat sequence participates in the disease process by producing neurotoxic substances and reducing the level of C9orf72 protein Recently, C9orf72, together with SMCR8 and WDR41, has been shown to regulate membrane trafficking, autophagy, and function as Rab GEF. However, the precise function of C9orf72 remains unclear. Here, we report the cryogenic electron microscopy (cryo-EM) structure of the human C9orf72-SMCR8-WDR41 complex at a resolution of 3.2 Å, unveiling the dimeric assembly of a heterotrimer of C9orf72-SMCR8-WDR41. Notably, the C-terminal tail of C9orf72 and the DENN domain of SMCR8 play critical roles in the dimerization of the two protomers of the C9orf72-SMCR8-WDR41 complex. In the protomer, while C9orf72 interacts with SMCR8 in a manner similar to the FLCN-FNIP2 complex, the GTPase activating protein (GAP) of RagC/D, WDR41 is connected to the DENN domain of SMCR8 through its N-terminal β-strand and C-terminal helix but does not directly interact with C9orf72. Structural comparison and sequence alignment revealed that Arg147 of SMCR8 is conserved and corresponds to the arginine finger of FLCN, and biochemical analysis indicated that the Arg147 of SMCR8 is critical to the stimulatory effect of the C9orf72-SMCR8 complex on Rab8a and Rab11a. Our study not only illustrates the basis of the C9orf72-SMCR8-WDR41 complex assembly but also reveals the GAP activity of the C9orf72-SMCR8 complex.

S8-1-8/12-3(18:15-18:30）

Hello, the era of intelligent microscopic imaging analysis

Tong Xin

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S7-1/12-3(16:15-16:35）

(Cancer) Theranostics with Radiolabeled Nanomaterials

Weibo Cai
University of Wisconsin-Madison, USA

S7-2/12-3(16:35-16:55）

可局部注射纳米药物研究进展

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S7-3/12-3(16:55-17:15）

铁基纳米药物及其肿瘤诊治

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目前，临床上正在使用的具有T1加权效果的Gd基磁共振成像（MRI）造影剂会引起肾囊纤维化等副作用。基于此，中科院宁波材料所的团队多年来一直致力于更加安全高效的铁基磁共振成像造影剂，同时基于铁元素的铁凋亡治疗和免疫治疗，同时基于铁基纳米材料的光热效果发展了一系列的铁基纳米诊疗一体化试剂。本报告中，将做系统性汇报。

S7-4/12-3(17:15-17:35)

TBD

Cong Li
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S7-5/12-3(17:35-17:55）

血管组织工程研究

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S7-6/12-3(17:55-18:15）

靶向肿瘤代谢/免疫互作的递药策略

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S7-7/12-3(18:15-18:30）

蛋白质药物胞内递送系统

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作用于胞内靶点的蛋白质药物可实现不同疾病的有效治疗。然而，目前临床上的蛋白质药物主要以细胞外靶点为主，这主要是由于蛋白质药物分子量大、亲水性强、易降解、难以渗透细胞膜，目前仍缺乏有效的蛋白质胞内递送载体和技术用于实现胞内蛋白治疗。考虑到蛋白质等电点差异大的特点，我们首先发展了蛋白质可逆负电化策略，制备了光控蛋白前药、乏氧自催化纳米酶原和类核酸化蛋白前药，从而实现了阳离子聚合物对负电化蛋白前药的高效包载和跨膜胞内递送，并通过响应活性氧自由基（ROS）、乏氧、低pH等信号，实现了蛋白质活性的可逆恢复[1,2]。我们进一步设计了富含苯硼酸的超支化聚（β-氨基酯），其可通过静电作用、疏水作用、氮-硼（N-B）配位等多重作用力实现对不同等电点和分子量的天然蛋白质的高效装载和胞内递送。聚合物主链中的苯硼酸还可在胞内双氧水作用下氧化并降解聚合物，从而有效释放蛋白质并发挥其药理活性[3]。最后，考虑到聚合物材料的潜在毒性、缺乏细胞选择性、内吞入胞易被溶酶体捕获等问题，我们开发了氨基酸转运体LAT1介导的无载体蛋白质胞内递送系统，通过ROS响应的苯硼酸连接键对蛋白质表面氨基进行LAT1底物修饰，可实现肿瘤细胞对蛋白前药的高效、选择性、不依赖内吞的高效摄取。该无载体化蛋白胞内递送平台可作用于一系列具有不同分子量和等电点的酶、毒素蛋白、抗体和用于基因编辑的核糖核酸蛋白[4]。

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S7-8/12-3(18:30-18:45）

纳米药物递送：从靶向到精准

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S7-9/12-3(18:45-19:00）

核酸药物的体内递送载体构建及应用研究

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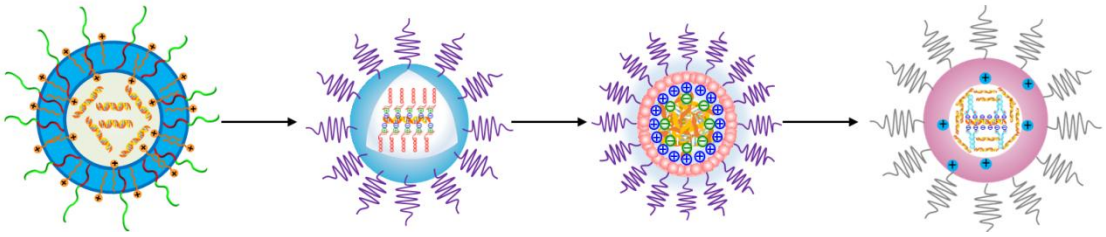
近年来，包括siRNA、mRNA等核酸药物的临床获批，在重大疾病治疗、新冠病毒预防等方面展现出独特的优势；而这些核酸类药物与以往药物不同，极度依赖于递送系统。

在前期研究中，我们利用限域组装的方法，实现了聚乳酸类纳米载体对siRNA的有效负载与体内递送，并在多种疾病模型上充分验证了该纳米体系的有效性。

此外，我们还利用含大疏水结构域化疗药物，将siRNA疏水化，进而通过聚乳酸类载体递送，避免使用阳离子材料，并实现了siRNA与化疗药物的同步递送。基于这些纳米体系，我们探讨了其在免疫-化疗协同治疗肿瘤方面的应用。



S7-10/12-3(19:00-19:20)

Lipid Nanoparticle-Mediated mRNA Delivery for CAR T Cell Engoneering

Michael Mitchell

University of Pennsylvania, USA

S7-11/12-3(19:20-19:40)

Development of Nanomaterials for mRNA Therapeutics, Genome Editing and Cell Therapy

Yizhou Dong

The Ohio State University, USA

S13-1/12-3(16:30-16:50)

HBV与宿主相互作用研究

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S13-2/12-3(16:50-17:10)

Vpr 通过拮抗限制性因子 LAPTM5 而促进 HIV 感染巨噬细胞

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HIV-1 编码一系列辅助蛋白对抗宿主细胞限制因子，如 Vif、Vpu 和 Nef 分别通过拮抗 APOBEC3G、Tetherin 和 SERINC5 促进 HIV-1 感染。Vpr 是一种进化上十分保守的辅助蛋白，为病毒在体内复制所必需，与患者高病毒载量和艾滋病疾病进展密切相关。研究发现 Vpr 可促进巨噬细胞和树突状细胞中 HIV-1 的复制已 30 余年，但机制至今未知。我们的研究发现：溶酶体相关跨膜蛋白 LAPTM5 是一种巨噬细胞特异性的新型宿主细胞限制因子，Vpr 通过拮抗 LAPTM5 促进巨噬细胞中 HIV-1 的复制。HIV-1 感染巨噬细胞后，Vpr 通过 DCAF1-DDB1-CUL4 E3 泛素化连接酶途径将 LAPTM5 转运到蛋白酶体降解，HIV-1 Env 得以从高尔基复合体分泌到细胞膜，用于 HIV-1 子代病毒的组装，从而增强 HIV-1 子代病毒颗粒的侵染能力和传播感染能力。而 Vpr 缺失时，LAPTM5 在高尔基体招募 HIV-1 Env 到溶酶体降解，子代病毒颗粒上的 Env 减少，进而显著降低其侵染能力。巨噬细胞构成了对入侵病原体的固有免疫和适应性免疫反应之间的重要桥梁，我们的研究阐明了 HIV-1 感染巨噬细胞后 LAPTM5 的抗病毒机制及其与 Vpr 的相互作用机制，为 HIV-1 如何逃避先天免疫提供重要见解，为 HIV/AIDS 的治疗提供新的策略和靶点。

S13-3/12-3 (17:10-17:30)

Vimentin inhibits α-tubulin acetylation via enhancing α-TAT1 degradation to suppress the replication of human parainfluenza virus type 3

Mingzhou Chen

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S13-4/12-3 (17:30-17:50)

Basic Research meets the Needs for Clinical Practice of Respiratory infectious Diseases

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Three coronaviruses have crossed species to cause severe human respiratory disease in the past 20 years, including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-2. Countermeasures for prevention and control of the pandemic, as well as to efficiently diagnose and treat the patients infected with these highly pathogenic coronaviruses are in urgent need.

Here, we summarize some of our previous studies that meet the needs for clinical practice when encountered respiratory infectious diseases. First of all, the disclose of transmission routes for a new emerging virus infection is critical, based on which the government could make efficient policy to stop virus spread and quickly quarantine close contacts. Our group first isolated SARS-CoV-2 virus in patient feces and urine, indicating SARS-CoV-2 could transmit through feces-oral route. We also revealed that in Africa, dromedary camels are the intermediate host for MERS and the patient numbers with asymptomatic MERS are dramatically underestimated. Then, we dissected the immunopathogenesis of these coronavirus infections. We found that virus-specific T cells, especially cells that are reside in the lungs are protective. In addition, humoral response not only could be used for diagnosis, but also is efficient for severe disease prognosis. Last, to end the pandemic, we need efficient and long lasting vaccines. We have developed the first Ad5-hACE2 mouse model for COVID-19, using which we were able to test variety of vaccine and drug candidates.

In summary, to prevent and control a pandemic cause by emerging respiratory virus infection quickly, researchers need to focus on the immediate needs of clinical practice.

S13-5/12-3(17:50-18:10)

新冠感染的免疫学特征及其免疫调节

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新冠感染导致的患者免疫功能紊乱，特别是免疫因子风暴导致的肺部炎症反应是患者出现严重阻塞性病变甚至死亡的重要原因，因此如何有效的降低新冠感染者炎症反应是控制病情进展的关键，我们利用基因修饰干细胞来源的外泌体以及食源性免疫调节剂，在新冠肺炎动物模型上证实了其有效性，为新冠肺炎的控制提供了证据。

S13-6/12-3(18:10-18:35)

Skin microbiota, odorants and arbovirus transmission

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Host-seeking activity of hematophagous arthropods is essential for arboviral transmission. Here, we demonstrate that mosquito-transmitted flaviviruses can manipulate host skin microbiota to produce a scent that attracts mosquitoes. We observed that *Aedes* mosquitoes preferred to seek and feed on mice infected by dengue and Zika viruses. Acetophenone, a volatile compound that is predominantly produced by the skin microbiota, was enriched in the volatiles from the infected hosts to potently stimulate mosquito olfaction for attractiveness. Of note, acetophenone emission was higher in dengue patients than in healthy people. Mechanistically, flaviviruses infection suppressed the expression of RELMα, an essential antimicrobial protein on host skin, thereby leading to expansion of acetophenone-producing commensal bacteria and consequently a high acetophenone level. Given that RELMα can be specifically induced by a vitamin A derivative, dietary administration of isotretinoin to flavivirus-infected animals interrupted flavivirus lifecycle by reducing mosquito host-seeking activity, thus providing a strategy of arboviral control.

S13-7/12-3(18:35-18:50)

The molecular characterization of the highly immunogenic SARS-CoV-2 nucleocapsid protein

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Severe acute respiratory distress syndrome-associated coronavirus-2 (SARS-CoV-2) nucleocapsid (N) protein is a highly immunopathogenic and multifunctional viral protein. At present work, we reported the crystal structure of SARS-CoV-2 nucleocapsid N-terminal domain (termed as SARS-CoV-2 N-NTD), as a model for understanding the molecular interactions that govern SARS-CoV-2 N-NTD binding to ribonucleotides. Compared with other solved CoV N-NTD, we characterized the specificity surface electrostatic potential of SARS-CoV-2 N-NTD. Additionally, we further demonstrated the unique RNA binding site characteristics. Our findings would aid in the development of new drugs that interfere with viral N protein and viral replication in SARS-CoV-2, and its highly related virus SARS-CoV.

Although human antibodies elicited by SARS-CoV-2 N protein are profoundly boosted upon infection, little is known about the function of N-directed antibodies. Herein, we isolated and profiled a panel of 32 N protein-specific monoclonal antibodies (mAb) from a quick recovery coronavirus disease-19 (COVID-19) convalescent, who had dominant antibody responses to SARS-CoV-2 N protein rather than to Spike protein. The complex structure of N protein RNA binding domain with the highest binding affinity mAb nCoV396 reveals the epitopes and antigen's allosteric changes. Functionally, a virus-free complement hyper-activation analysis demonstrates that nCoV396 specifically compromises N protein-induced complement hyper-activation, a risk factor for morbidity and mortality in COVID-19, thus paving the way for functional anti-N mAbs identification.

S10-1/12-3(16:30-16:50)

A comparative study of hypoxia, hyperoxia and exercise health

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Purpose:
Tn order to reveal the hot dynamics and frontier issues in hypoxia and hyperoxia research, to further understand the value of hypoxia and hyperoxia research and applications, and to better apply hypoxia and hyperoxia therapy to the promotion of chronic disease prevention and human health.
Methods:
Extracts from the Web of Science (WOS), MEDLINE, EMBASE, Cochrane and Effectiveness Review databases were searched by the bibliographic method using the following terms. "Hypoxia", "Hyperoxia", "Chronic disease", "Health". Systematic review of hypoxia and hyperoxia research and development. And use Citespace software to explore the research and development progress of global hypoxia and hyperoxia.
Results:
The number of publications on hypoxia research has grown rapidly in recent years, with Western countries having more research in this area and China still having little influence in the world in this area. The use of mild hypoxia, or hypoxia conditioning , to strengthen the resilience of organs or the entire body to severe hypoxic insults is an important preparation for high-altitude sojourns or to protect the cardiovascular system from hypoxia/ischemic damage is already a cornerstone of modern medicine. Many more hypoxia and/or hyperoxia adaptations are still in the early stages of development. HC is gaining popularity for the treatment of chronic illnesses, including obesity, diabetes, hypertension, and promote active health. It is sometimes used in conjunction with hyperoxia therapies.
Conclusions:
The field of hypoxia and hyperoxia are developing rapidly, and innovative applications, such as controlling the aging process, chronic disease prevention and health promotion, hypoxia and hyperoxia are increasingly recognized. More research is needed on the effects of altering the intensity, duration, and frequency of oxygen concentrations, and individual susceptibility to such treatments, to develop hypoxia/hyperoxia training into therapeutic applications.

S10-2/12-3(16:50-17:10)

Advances in Highland Sports Medicine Research

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Hypoxia is a challenge to human beings on the plateau. The significant plateau hypoxic environment will due to failure of human body to adapt to the plateau environment cause human physiological dysfunction or pathophysiological changes, resulting in hypoxic injury and plateau decline, leading to the overall decline of human mental and physical strength and the occurrence of various types of acute and chronic plateau diseases, reducing the quality of life, not only affecting health but also endangering life.

The most active and effective way for humans to adapt to the plateau is to exercise. Studies have shown that the mild hypoxia of a moderate plateau (1500~3000m above sea level) can play a role in "activating" the physiological functions of the human body. This improves heart, lung and blood functions, enhances oxygen utilization and improves metabolism, bringing beneficial effects to the organism and health. Highland climate superimposed on physical exercise to improve heart and lung function and health, alpine recuperation and highland health tourism as well as highland training in competitive sports have become important means to improve health and sports competition today, and are also a hot spot for research worldwide.

As plateau exercise belongs to the science of the environment and the role of exercise on the human body, plateau exercise or exercise the human body to withstand the dual stimulation of environmental low oxygen and load low oxygen, the organism changes more complex and profound. Therefore, it is of great significance to strengthen the research on the effects of exercise and exercise in hypoxic environment on human hypoxic adaptation and physiological functions, as well as the methods and means to adopt scientific exercise tests and exercise prescriptions, to guide plateau sports and exercise, to effectively use hypoxic factors to improve athletic ability and promote human health, to prevent and treat chronic diseases, and to reduce the damage caused by the special environment of plateau to human body in the process of sports. It is also important to reduce injuries caused by the highland environment.

PSM (Plateau Sports Medicine) is a comprehensive and interdisciplinary discipline that includes plateau medicine, sports medicine, exercise physiology and sports training, etc. It focuses on the medical problems related to sports in plateau, alpine, mountainous and different geographical and climatic environments, and guides sports through medical means and technical supervision. The aim is to reduce the damage caused by the highland environment and to improve performance and health through the use of low oxygen. The main content includes physiological adaptation mechanisms in plateau sports, plateau training, plateau fitness sports and physical health, fatigue recovery and injury prevention in plateau sports, plateau training and low oxygen training. The service targets are national fitness, competitive sports, medical and health care, national defence construction, emergency rescue, scientific research, etc.

S10-3/12-3(17:10-17:30)

运动保护心脏的“一石三鸟”效应

肖俊杰

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从运动心脏中鉴别的靶点可以通过“一石三鸟”的效应保护心脏。我们通过对游泳训练小鼠左心室LncRNA芯片筛选结合荧光定量PCR检测发现LncRNA FR236703显著上调，将其命名为心脏生理性肥厚相关调控分子(Cardiac Physiological hypertrophy associated regulator, CPhar)。过表达CPhar可促进心肌细胞肥大和增殖，抑制氧葡萄糖剥夺恢复所致的心肌细胞凋亡。在动物水平研究表明，CPhar为运动介导心脏益处所必需，抑制CPhar表达，游泳训练的小鼠将不能发生生理性心肌肥厚；增加CPhar可以改善心肌缺血再灌注损伤所致的心室重构和心功能异常。机制研究发现，ATF7是CPhar发挥功能的关键下游分子。进一步采用质谱分析、RNA沉降、RNA结合蛋白免疫沉淀、染色质免疫沉淀、荧光素酶报告实验及免疫共沉淀等方法揭示，CPhar通过结合RNA解旋酶DExD/H-box家族蛋白17（DDX17），特异性螯合生理性心肌肥厚关键转录因子C/EBPβ调控其下游分子ATF7。

S10-4/12-3(17:30-17:50)

Using Drosophila as a Model: Exercise Health Promotion in Aging Heart

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Exercise can delay age-degenerative changes in cardiac structure and function, and its molecular basis and potential molecular protective pathways remain unclear. The model animal Drosophila has attracted attention in the field of aging research because of its short life cycle, sophisticated transgenic technology, and abundant phenotypes. Based on the behavioral characteristics of Drosophila climbing against gravity, we developed the Drosophila exercise training device, innovatively established the Drosophila exercise model, introduced and improved the research methods for Drosophila cardiac structure and function, and investigated the changes of heart structure and function during physiological aging, as well as established a high-sugar/high-fat diet-induced pathological heart aging model, and studied the molecular pathways of hypoxia and/or exercise to improve cardiac health. Our study revealed that hypoxia and/or exercise ameliorated aging or high-fat diet-induced lipotoxic cardiomyopathy, enhanced exercise capacity and prolonged healthy lifespan in Drosophila through activation of NAD+/dSIR2/PGC-1α pathway, dSIR2/FOXO/SOD pathway and dSIR2/FOXO/Bmm pathway, as well as downregulation of apoLpp expression in cardiomyocytes. In addition, the dSIR2/Cyc pathway was found to be key molecules mediating exercise delayed age-dependent sleep-wake rhythm disturbances and cardiac arrhythmias.

S10-5/12-3(17:50-18:10)

低氧诱导外泌体参与结直肠癌转移的机制探讨

Rui Chen

Capital Medical University, China

S10-6/12-3(18:10-18:25)

A Review of Epidemiological Studies on Genomic longevity and aging

Dianjianyi Sun

Peking University

S10-7/12-3(18:25-18:40)

Regulation of chromatin states and conformations during heat shock response in mammalian cells

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Heat shock is a common environmental stress, while the response of the nucleus to it remains controversial in mammalian cells. Acute reaction and chronic adaptation to environmental stress may have distinct internal rewiring in the gene regulation networks. However, this difference remains largely unexplored. Here, we report the different responses of chromatin conformation, chromatin accessibility and nucleosome positions in short- and long-term heat shock in a common model system—human K562 cells. We found that chromatin conformation in K562 cells was largely stable in response to short heat shock, while it showed clear and characteristic changes after long-term heat treatment with little alteration in chromatin accessibility during the whole process. We further showed in silico and experimental evidence strongly suggesting that changes in chromatin conformation may largely stem from an accumulation of cells in the M stage of cell cycle in response to heat shock. This conclusion was further supported by the similarity of stability and variability of chromatin accessibility profiles between heat shock and transition of cells from G1/S phase to G2/M phase. Nucleosomes were globally removed in genome regions which respond to heat shock, no matter the direction of the responses, which also differed from the observations in poikilotherms such as yeast or Drosophila. Our results represent a paradigm shift away from the controversial view of chromatin response to heat shock and emphasize the necessity of cell cycle analysis when interpreting bulk Hi-C data. It also supplied evidences to the new opinion that nucleosome positionings controlled responsiveness of regulatory elements, not the regulation direction, in mammalian cells.

S10-8/12-3(18:40-18:55)

The Joint Effect of $PM_{2.5}$ Exposure and Physical Activity on Cognitive Function and Hemodynamic Response: A fNIRS study

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Background: Previous studies indicate that $PM_{2.5}$ exposure may adversely affect respiratory and cardiovascular systems. In recent years, it has been found that $PM_{2.5}$ exposure may lead to cognitive impairment. However, the interaction of $PM_{2.5}$ exposure and physical activity on cognitive function and its hemodynamic mechanism have not been reported.

Methods: This study explored the interaction between $PM_{2.5}$ exposure and physical activity on cognitive function through the national population sample of China family follow-up survey (CFPS). In order to further explore the causal relationship and the underlying mechanism of hemodynamics, we also conducted a randomized controlled trial study (RCT), with $PM_{2.5}$ purified and exercise interventions, to explore the interaction of $PM_{2.5}$ exposure and physical exercise intervention on cognitive function and the hemodynamic response mechanism of prefrontal cortex using the functional near-infrared spectroscopy (fNIRS).

Results: We found that $PM_{2.5}$ exposure had adverse effects on cognitive function (β = -0.084, 95%CI: -0.109, -0.06) in CFPS. PA and $PM_{2.5}$ exposure had an interactive effect on cognitive function(β=- 0.037, 95%CI：-0.045，-0.029). In the RCT study, we found that high-intensity intermittent exercise (HIIT) could improve the response time of consistent Stroop task by 87% (β = 0.872, 95%ci:0.779, 0.976), and increased the response time of inconsistent Stroop tasks by 88% (β = 0.886, 95%CI: 0.815, 0.964) compared with the control group. $PM_{2.5}$ exposure and HIIT have interactive effects on the response time of consistent and inconsistent Stroop tasks. This indicates that HIIT intervention can improve cognitive function. However, the benefits of HIIT may be attenuated under high concentrations of $PM_{2.5}$ exposure. HIIT, moderate-intensity of continuous training (MICT), and $PM_{2.5}$ had effects on the hemoglobin concentration in the dorsolateral superior frontal gyrus.

Conclusion: $PM_{2.5}$ exposure and physical activity have interactive effects on cognitive function, which HIIT was better than MICT. The activation of the dorsolateral superior frontal gyrus may be the hemodynamic response mechanism of $PM_{2.5}$, and exercise affecting cognitive function.

Keywords: $PM_{2.5}$ Exposure; Physical activity; Cognitive function; Hemodynamic response; fNIRS

S10-9/12-3(18:55-19:10)

A comparative study on the characteristics of plantar pressure of high altitude native and immigrant college students

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Objective: To investigate the characteristics of plantar pressure of college students who are native Tibetan and immigrated Han residents in Tibet University.

Methods: All native Tibetan and immigrant Han college students from grade one class of clinical medicine were selected by cluster sampling method. The MPS flat panel test system (Loran, Italy) was used to test the gait during static standing and dynamic walking. SPSS 24.0 was applied for the data entering and analysis . Data were reported as（$x\pm s$）.Difference in mean values between two ethnic group was tested using T-test. The level of statistics significance was set at $p<0.05$.

Results: There were differences in 17 out of 21 of measured parameters between two compared groups, such as peak pressure, average pressure, single foot touchdown time, gait cycle, foot axis angle, contact area of each region, pressure peak of each region, proportion of stress time of each region, average pressure of each region, etc.

Conclusion: The results of the present study suggest that mastering the characteristics of plantar pressure in specific group can provide a scientific basis for the application research of plantar pressure in different ethnic populations, so as to guide physical exercise, rehabilitation training, as well as the shoes design and manufacture.

PL-4/12-4(8:30-9:15)

仿生合成疫苗：从人工颗粒到天然颗粒底盘

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疫苗不仅用于预防重大传染病，而且在肿瘤等重大疾病的治疗有着巨大的潜力。因此，理想的疫苗是能同时诱导体液和细胞免疫应答。传统减毒和灭活疫苗可诱导高效体液免疫应答，但存在灭活不彻底或毒力恢复等安全隐患，而且用传统铝佐剂无法提高细胞免疫应答。使用亚单位抗原（病毒样颗粒VLP、蛋白、多肽等）的疫苗安全性明显提升，但却存在着疫苗稳定性差、免疫原性弱、细胞免疫应答低的关键难题。

1）我们提出仿生颗粒的思路，用简单的Pickering乳液模仿病毒、细菌等病原体的特征，作为合成疫苗的“底盘”，与不同的抗原（部件）组装，构建更稳定、高效且能大规模生产的合成疫苗，同时提高了体液免疫和细胞免疫密，且免疫效果远优于普通颗粒。

2）提出利用天然颗粒制备以外泌体为底盘的双靶向肿瘤疫苗的策略，用于肿瘤的个体化精准治疗。从病人肿瘤组织获得个体化肿瘤细胞核，用巨噬细胞吞噬肿瘤细胞核，获得杂化细胞，再用佐剂刺激细胞获得嵌合外泌体，外泌体表面携带肿瘤抗原肽，肿瘤黏附因子等，还携带巨噬细胞的信息。因此，该疫苗通过黏附因子靶向肿瘤组织改善肿瘤微环境，通过巨噬细胞的信息靶向淋巴结激活特异性免疫应答，通过双管齐下作用，获得了优异的肿瘤治疗和预防复发效果。

PL-5/12-4(9:15-10:00)

脑发育与演化的分子细胞调控机制

Xiaoqun Wang

Beijing Normal University

PL-6/12-4(10:15-11:00)

TBD

Maili Liu

Innovation Academy for Precision Measurement Science and Technology, CAS

S1-2-1/12-4(13:30-13:50）

TBD

Zhiwei Huang

Harbin Institute of Technology, China

S1-2-2/12-4(13:50-14:05）

Structural mechanisms of TRPV2 modulation by endogenous and exogenous ligands

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Transient receptor potential vanilloid 2 (TRPV2) ion channel is a polymodal receptor broadly involved in many physiological and pathological processes. Despite many TRPV2 modulators identified, whether and how TRPV2 is regulated by endogenous lipids remains elusive. Here we found an endogenous cholesterol molecule inside the vanilloid binding pocket (VBP) of TRPV2, with a ‘head down, tail up’ configuration, resolved at 3.2 Å by cryo-EM. Cholesterol binding antagonizes ligand activation of TRPV2, which is removed from VBP by methyl-β-cyclodextrin (MβCD) as resolved at 2.9 Å. We also observed that estradiol (E2) potentiated TRPV2 activation by 2-Aminoethoxydiphenyl borate (2-APB), a classic tool compound for TRP channels. Our cryo-EM structures (revolved at 2.8-3.3 Å) further suggested how E2 disturbed cholesterol binding and how 2-APB bound within the VBP with E2 or without both E2 and endogenous cholesterol, respectively. Therefore, our study has established the structural basis for ligand recognition of the inhibitory endogenous cholesterol and excitatory exogenous 2-APB in TRPV2.

S1-2-3/12-4(14:05-14:20）

Architecture of Outer Rings From *Xenopus laevis* Nuclear Pore Complex Obtained By Cryo-EM and AI

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The nuclear pore complex (NPC) is one of the largest protein complexes in eukaryotes, performing multiple roles in cell life, including mediating nucleocytoplasmic transport. Solving its sophisticated architecture could be essential for the understanding of this fundamental assembly. Most recently, we used NPCs on *Xenopus laevis* oocyte nuclear envelope as target, imaged NPCs as top-view particles on flattened nuclear envelope and side-view particles on the edge of folded back nuclear envelope, by an integration of cryo-SPA and artificial intelligence (AI) methods, we obtained the fine structure of the outer rings from *Xenopus laevis* NPC up to 8 Å resolution, with local resolution reaching 4.9 Å, the reconstructions were nearly isotropic. Based on structure features of electron density maps and predictions of full-length structures of all outer ring nucleoporins by AlphaFold2, we built the pseudo-atomic model of NPC outer rings, composed of around 33,400 amino acids, reaching nearly 33MDa.

With this model, we have fulfilled the previously absent gap in the hub region of Y complex, described the full interaction network within the Y complex in outer rings. Furthermore, we have distinguished and modeled five copies of Nup358, two copies of Nup214 complex and one copy of Nup93 in each cytoplasmic ring (CR) asymmetric unit, one copy of Nup205, one copy of ELYS and one copy of Nup93 in each nuclear ring (NR) asymmetric unit. We further modeled Nup205 in CR and ELYS in NR and confirmed their locations. With all the advances mentioned above, we have successfully established nearly completed interaction network of outer ring members.

In all, based on higher resolution reconstruction and more complete atomic model of outer ring of *Xenopus laevis* NPC, we have revealed interaction networks within outer ring components in metazoans, providing structural bases for further understanding of metazoan NPC’s structure, assembly and functions.

S1-2-4/12-4(14:20-14:35)

Keep your particles well-behaved: Graphene support to boost Cryo-EM analysis

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High-quality and controllable specimen preparation is now still a practical challenge in cryo-EM field, which is impaired by the air-water interface, strong background noise, particles' preferential orientation and beam-induced motion problems. Aiming to achieve a more reproducible cryo-EM specimen preparation and keep the target particles "well behaved" in the vitreous ice, a new generation of supporting films has been explored in recent years. Graphene with the superior properties of ultrahigh electrical/thermal conductivity, mechanical strength and negligible background noise, is considered as an ideal supporting film in cryo-EM. Here we reported several graphene-based supporting films, including ultraflat graphene, functionalized graphene with various charges or affinity ligands, and graphene sandwich structure to encapsulate biomolecules. We found these membranes enabled more controllable ice thickness during specimen preparation. Small-molecular-weight biomolecules exhibited nice contrast on these membranes and could be reconstructed at near atomic resolution. Moreover, the majority of particles were found to be absorbed onto the membrane surface with rich orientations, thus avoiding the air-water interface and preferential orientation problems. We envision that these graphene-based membranes have great potentials as robust supporting films for high-resolution cryo-EM analysis.

S1-2-5/12-4(14:35-14:55）

Cryo-EM study of CatSpermasome—a sperm channel-transporter supercomplex

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S1-2-6/12-4(15:10-15:30）

植物小RNA生物合成的分子机制研究

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DNA甲基化（5mC）是真核生物中保守的表观遗传调控方式，在基因沉默、基因组印记、抵御病毒入侵等多种生物学功能中发挥着重要的作用。在植物中，DNA甲基化和组蛋白H3K9me2修饰可以形成正反馈循环而在染色质上维持并扩增DNA甲基化，其边界的维持需要DNA主动去甲基化的协助来实现。与动物中依赖于TET和TDG两类酶引导甲基化位点缺失进入DNA修复完成主动DNA去甲基化不同，植物仅需要ROS1/DEMETER家族一类酶即可完成甲基化DNA切除，从而直接进入DNA修复开展DNA去甲基化，但ROS1家族蛋白富含无规卷曲，限制了其结构生物学研究的开展。本研究中，我们对植物DNA去甲基化酶ROS1的催化区开展了大量的蛋白改造，利用突变、截取、融合DNA作用蛋白等多种手段结合的方式，成功获取了ROS1与其底物甲基化DNA的稳定复合物，利用冷冻电镜技术成功解析了该复合物的结构。复合物中，ROS1呈现出经典的DNA glycosylase/lyase双功能酶的构像，甲基化胞嘧啶被翻转插入ROS1的碱基结合口袋，并产生特异性识别。此外，ROS1也可以切除T:G mismatch DNA中的T，尽管活性略低，我们通过结构测定显示，尽管T和5mC整体上非常类似，但是在碱基第三位的质子化状态的不同，造成了ROS1对5mC的偏好性切割。整体上，我们解析了植物ROS1家族DNA去甲基化酶的多种复合物结构，阐释了其直接识别和切割5mC的机制。

S1-2-7/12-4(15:30-15:45)

Cryo-EM structures of TMEM106B fibrils extracted from FTLD-TDP patients

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FTLD (Frontotemporal lobar degeneration) is the third most common neurodegenerative condition, following Alzheimer's and Parkinson's diseases. FTLD tends to present in 45-64-year-olds and is broadly presented as behavioral or language disorders. The major subtype FTLD-TDP (FLTD with TAR DNA-binding protein inclusions) contributes to ~50% of the FTLD cases, and is characterized by certain clinical symptoms and pathological inclusions detected by TDP-43 immunoreactivity. Here we extracted amyloid fibrils from brains of four patients, representing four out of five FTLD-TDP subclasses and determined their near-atomic resolution structures via cryo-EM. Unexpectedly, all amyloid fibrils examined are composed of a 135-residue C-terminal fragment of TMEM106B, a lysosomal membrane protein previously implicated as a genetic risk factor for FTLD-TDP. Three-dimensional reconstructions suggest all patient-derived fibrils are composed of one or two protofilaments with a stable, conserved, golf-course-like fold. Further western blot and immunogold labeling assays suggest that TDP-43 forms non-fibrillar aggerates in these patients. Our study confirm that FTLD-TDP is an amyloid-involved disease and suggest that amyloid involvement in FTLD-TDP is of protein TMEM106B, rather than of TDP-43. Our findings will refocus attention on the pathogenic role of this largely ignored protein, and perhaps open a pathway to structure-based therapies for this common form of brain degeneration.

S1-2-8/12-4(15:45-16:00）

SNX27-FERM-SNX1 complex structure rationalizes divergent trafficking pathways by SNX17 and SNX27

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The sorting nexin proteins are critical for endosomal trafficking and signaling. SNX17 and SNX27 are two SNX proteins displaying high similarity in domain structure, including a common FERM domain; however, they mediate distinct endocytic recycling pathways. We now solve this mystery by demonstrating that the FERM domains of SNX17 and SNX27 have different functions. Whereas the FERM domain of SNX17 recognizes the NPxY/NxxY motif, the same domain in SNX27 binds to a novel “DLF” motif within the N termini of SNX1/2. The interaction between SNX27 and SNX1/2 not only helps efficient retrieval of multiple cargoes but also promotes endosomal recruitment of SNX27. We further demonstrate that the SNX27-SNX1/2 interaction is crucial to neuronal growth and brain development in zebrafish. Altogether, our study solves a long-standing puzzle in the field and suggests that SNX27 and SNX17 mediate endocytic recycling through fundamentally distinct mechanisms.

S1-2-9/12-4(16:00-16:15)

A direct method to solve protein crystal structures from X-ray diffraction data with iterative projection and deep learning algorithms

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Atomic-resolution protein structures are usually determined from X-ray diffraction pattern. Although AlphaFold and RoseTTAFold could predict most protein structures at various confidence levels, the true atomic structure of a protein still needs to be determined and checked by experiment. Determining the phases of the diffraction pattern is crucial since the diffraction pattern only records the diffraction magnitudes. We proposed a direct phasing method to solve protein crystal structures from X-ray diffraction data. The method starts from random phases without any prior information about the structure which makes it free of model bias. The basic version of the method consists of iterative projection algorithms such as hybrid-input output (HIO) algorithm and histogram matching technique, which works well on phasing protein crystals with high solvent content. For intermediate solvent content crystals, it becomes difficult to reconstruct the protein envelope from scratch, which is essential for solving the atomic structure. A transition region between the protein and the solvent was introduced to refine the reconstructed protein envelope. Iterative projection algorithms, such as continuous hybrid-input output (CHIO) and hybrid-projection reflection (HPR), are able to make use of the solvent inside the protein envelope during phasing the diffraction data, which help a lot in dealing with intermediate and low solvent-content crystals. For phasing low solvent-content crystals, non-crystallographic density averaging was used to determine atomic structures. In addition, deep neural networks, such as deep convolutional neural network (DNN) and generative adversarial network (GAN) were trained by synthetic diffraction data and used to predict the protein envelope directly from the diffraction data. We tested our method on tens of protein structures which have been posted in the protein data bank (PDB). The retrieved phases of the method usually have a mean phase error around 30 degrees. The calculated density map is quite interpretable and the reconstructed structure matches well with the PDB posted model. The new phasing method can supplement and enhance the traditional phasing method and refinement tools. It is also quite useful for phasing X-ray free-electron laser (XFEL) diffraction data.

S1-2-10/12-4(16:15-16:35)

General approach to design of miniprotein binders to arbitrary protein targets

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Protein-protein interaction plays a key role in almost all the fundamental life processes, such as virus infection, immune recognition and cell signaling transduction. Designing de novo proteins that could specifically interact with native proteins has shown great potential for drug development and new diagnostic tools. Historically, binder design methods relayed on the information of binding hotspots or binding motifs derived from the complex crystal structures. The ability to design protein binders without using any of the native complex information could broadly expand the horizon of "computationally targetable" protein targets. I will present a method to design de novo protein binders to natural targets where the only information required is the target structure. Successful application of this method to several natural proteins will be shown, including designing picomolar miniprotein inhibitors that could neutralize the SARS-CoV-2 virus. More generally, the approach now enables targeted design of binders to sites of interest on a wide variety of proteins for therapeutic and diagnostic applications.

S1-2-11/12-4(16:35-16:43）

告别昂贵维护和浓度梯度-基于光栅耦合波导干涉的分子互作动力学分析技术

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非标记分析技术如表面等离子体共振（SPR）等已经广泛的被学术界用于基础科研以及药物研发中的分子间相互作用分析。然而，其高昂的维护保养费用、繁琐的样品浓度梯度配制以及无法分析弱相互作用的动力学信息一直阻碍着高校、研究机构有效的开展相关实验，同时也使药企难以获取评价部分稳态结合的小分子药物的动力学信息。基于波导结构的光栅耦合干涉仪（GCI）如WAVE系统，不仅在灵敏度上完全媲美甚至超越SPR，更因其独特的芯片流池设计和单一浓度动力学（WaveRAPID）的实验模式，创新的解决了SPR高昂的后期维护成本，提升了动力学分析的时间分辨率，减轻了分子互作分析人员前期样品配制的工作量，减少了浓度稀释的人为误差，大大缩短了分子互作的整体分析时长。

S8-2-1/12-4(13:30-14:00）

情感和情感障碍的神经环路研究

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S8-2-2/12-4(14:00-14:30）

恐惧情绪与睡眠环路

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S8-2-3/12-4(14:30-15:00）

靶向视觉系统调控疼痛的神经环路机制

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S8-2-4/12-4(15:00-15:30）

下丘脑神经内分泌系统的结构与功能解析

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S8-2-5/12-4(15:30-16:00）

Combinatorial genetic dissection of neural circuits

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The mammalian brain is composed of diverse neuronal cell types derived from neural stem cells. Genetic strategies engaging the intrinsic gene regulatory mechanisms that generate and maintain cell type identity allow precise and reliable identification and manipulation of cell lineages and cell types. Here we will present some recent work in developing combinatorial strategies incorporating two orthogonal recombinases to enhance specificity and flexibility of genetic targeting, lineage tracing and conditional gene regulation. We are applying these tools to decipher complex genetic architecture of brain disorders and uncover organization principles of neural circuits.

S8-2-6/12-4(16:00-16:30)

A vagal-NTS pathway that stimulates feeding

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A fundamental question of physiology is how gut-brain signaling stimulates appetite. While many studies have emphasized the importance of vagal afferents to the nucleus of the solitary tract (NTS) in inducing satiation, little is known about whether and how the vagal-NTS pathway senses orexigenic signals and stimulates feeding. Here, we reported a previously uncharacterized population of fasting-activated catecholaminergic neurons in the NTS. After characterizing the anatomical complexity among NTS catecholaminergic neurons, we surprisingly found that activation of NTS epinephrine (E^{NTS}) neurons that co-express neuropeptide Y (NPY) stimulated feeding, whereas activation of NTS norepinephrine (NE^{NTS}) neurons suppressed feeding. Monosynaptic tracing/activation experiments then showed that these NTS neurons receive direct vagal afferents from Gut-innervating nodose neurons. Moreover, Activation of the vagal-NPY/E^{NTS} neural circuit stimulated feeding. Our study reveals a vagal-NTS pathway that stimulates feeding.

S12-1/12-4(13:30-13:55)

Elastin-like polypeptide fused protein drugs

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Therapeutic proteins are widely used in clinic for the treatment of various diseases. Nevertheless, they often have short circulatory half-lives. As a result, frequent administrations at high concentrations are necessitated to achieve a therapeutically useful blood level, giving rise to not only heavy financial burden and poor compliance of patient but also unsatisfactory therapeutic efficiency and serious side effects. Conjugating synthetic polymers like poly(ethylene glycol) (PEG) with therapeutic proteins to yield protein-polymer conjugates is the most frequently used strategy to prolong the circulatory half-lives. So far, 20 PEGylated protein drugs have been used in clinic in the world. However, PEGylation has some disadvantages as follows: 1) PEG itself does carry some potential safety risks, such as the antibody formation against PEG and hypersensitivity to PEG; 2) Decreased activity and heterogeneity are also the negative aspects of PEGylated proteins, which may limit the wide use of PEGylated proteins. To address these challenges, we have combined protein engineering with polymer engineering to develop new and general strategies of site-specific in situ polymerization (SIP) and elastin-like polypeptide fusion (ELPfusion) to site-specifically modify proteins with polymers to form site-specific protein-polymer conjugates with well-retained bioactivity and high efficiency. In this presentation, I will talk about our recent progress in the design of ELP fused proteins for cancer therapy.

S12-2/12-4(13:55-14:20)

A Nanocomposite-based Vascularized Elastic Conductive Patch for the Repair of Infarcted Myocardium

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The integrity of conductivity, elasticity and fully vascularization into a cardiac patch remains a challenging. The prevascularization of conductive elastic cardiac patches could be an effective strategy for building a substantial connection between the patch and the infarcted heart. Here, we introduced a coronary artery casting into a holey graphene oxide/polypyrrole(hGO/pPy) nanocomposite-incorporated polyhydroxyethyl methacrylate prefabricated gel to form a vascularized conductive elastic patch. The introduction of a hGO/pPy conductive nanocomposite into the cryogel and the cryo-polymerization technique simultaneously achieved high conductivity as well as elasticity and toughness. Meanwhile, the 3D biomimetic vascular channels produced using prefabricated vascular casting templates helped to fully vascularize the cryogel in the dynamic culture. The vascularized, conductive, and elastic patch also can promote the functionalization and synchronous contraction of cardiomyocytes. Besides, the pre-vascularized network in the cryogel can guide cardiomyocytes' growth and penetration in the gel. After the vascularized conductive elastic patches are transplanted onto the rat's infarcted heart for 4 weeks, the changes of the left ventricular fractional shortening is elevated by 18% and that the infarcted area is decreased by 32% compared to the the MI group. Besides, The engineered patches were able to rebuild functional vascular anastomoses and provide strong electrical integration with infarcted hearts, resulting in effective myocardial infarction repair in vivo. RNA sequencing analyses further revealed that the conductive elastic patches under dynamic culture conditions upregulated cardiac muscle contraction- and ATP biosynthesis-related mRNA expression in vitro. Together, this study demonstrates that the fabricated patches have versatile conductivity, elasticity, and vascularization properties, and could therefore be a promising candidate for heart repair.

S12-3/12-4(14:20-14:45)

Self-assembled small-molecule prodrug nanomedicines in cancer therapy

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Chemotherapy is one of the most effective strategies in cancer treatment. Prodrug-based self-assembled nanoparticles (NPs), which integrate the advantages of prodrug strategy and nanocarriers, have emerged as an efficient drug delivery system (DDS) for cancer therapy. Prodrug nanoassemblies have the advantages of high drug loading, good stability and low toxicity, which have been widely studied in recent years.

Based on these, we have carried out the following work: (1) the disulfide bond-bridged prodrug nanoassemblies were demonstrated distinct redox responsibility. Instead of its previous application as a reduction-responsive bond, this work has greatly expanded the application of the disulfide bond as a chemical bridge for prodrugs. (2) a novel trisulfide bond-bridged DOX dimeric prodrug was designed and synthesized. The trisulfide bond has three sulfur atoms and two sulfur-containing dihedral angles, which significantly improve the self-assembly of DOX dimeric prodrug. Therefore, the colloidal stability, pharmacokinetics and tumor accumulation of the prodrug nanoassemblies were greatly improved.

S12-4/12-4(14:45-15:10）

动态PET定量成像技术

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S12-5/12-4(15:25-15:50)

Highly sensitive nanoprobes for medical imaging and therapy

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The rapid development of nanotechnology promotes the design and fabrication of high-performance imaging probes for biomedical applications [1]. Based on the important role of ions in life activities and disease early development, high-performance nanoprobes in response to certain ions (H^+, K^+, ROS, etc.) are designed via controlled chemical assembly for highly sensitive and specific imaging as well as efficient therapy for diseases [2]. The imaging or/and therapeutic functions of ion-responsive nanoprobes were elucidated under the disease microenvironment with abnormal ion levels [3]. The mechanism of ion-triggered biological function activation or amplification of ion-responsive nanoprobes has been investigated [4]. Overall, new strategies for are developed for the design of intelligent biomaterials for precise diagnosis and treatment, promoting interdisciplinary integration [5].

Keywords: nanoprobes; intelligent biomaterials; biomedical imaging; nanomedicine

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S12-6/12-4(15:50-16:15)

Metal-Phenolic Network (MPN) biomaterials for cancer therapy

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Introduction: Metal polyphenols networks (MPN), which make use of the coordination between metal ions and phenolic molecules, have emerged as promising materials for nanomedicine. Compared with other materials, MPNs have several potential advantages, including pH responsiveness, negligible cytotoxicity. Additionally, the phenolic groups in the materials can be functionalized to meet specific applications.

Methods and Result: We constructed a serious of polyphenol-based nanoplatform for combination cancer immunotherapy. These nanoplatforms were stable under normal physiological environment and release therapeutic agents in the tumor site. The MPN can enhance anti-tumor immune response by various strategies by exploiting the tumor microenvironment.

Conclusion: MPN based nanoplatforms can evoke highly efficacious cancer immunosurveillance while minimizing systemic side effects.

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S12-6/12-4(16:15-16:30）

雄黄纳米晶在髓系白血病治疗中的应用及机理研究

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研究背景和目的：雄黄在血液肿瘤治疗中的应用起始于上世纪60年代左右，已展现出一定的治疗效果，但临床应用仍然面临两方面的限制：其一，由于雄黄水溶性很差，为了获得有效的血药浓度需要大量服用，给患者带来健康和经济负担；其二，由于仅能溶解于氢氧化钠溶液形成混合形式的砷盐，雄黄（As_4S_4晶体颗粒）的药理仍没有完全阐明。本研究的目的是提高雄黄水溶性，增加雄黄的生物利用度，并在此基础上研究雄黄对白血病的作用机理及其治疗效果。

方法和结果：通过热熔共挤出技术制备两亲性高分子包被的雄黄纳米颗粒（e-As_4S_4），通过动态光散射、扫描电镜等观察纳米颗粒的粒径分布。
与雄黄原粉相比，e-As_4S_4中雄黄晶体的颗粒直径由数十微米减小至470 nm，纳米制剂可在水中崩解形成黄色胶体溶液。e-As_4S_4以纳米晶的形式被细胞摄取，与雄黄原粉相比，其生物利用度提高12.6倍，细胞毒效率提高177倍。在此基础上开展了雄黄对白血病细胞作用机理的系统研究。结果表明，e-As_4S_4通过其还原性及线粒体呼吸抑制导致胞内活性氧（ROS）降低，一方面引起自噬性的BCR-ABL降解，诱导人慢性髓细胞白血病细胞系和患者骨髓来源的单个核细胞发生红系分化；另一方面抑制组蛋白乙酰化酶活性，增加*RUNX1*的转录，诱导慢性髓系白血病细胞发生巨核系分化。在难治性急性髓系白血病细胞和小鼠模型中，e-As_4S_4也通过抑制组蛋白乙酰化酶活性，增加*RUNX1*，*GATA1*，*CEBPA*，*SPI1*等基因的转录，诱导急性白血病细胞的多系分化，从而诱导白血病细胞的分化后凋亡，延长小鼠生存时长。此外，连续14天给予健康小鼠治疗剂量的e-As_4S_4后，小鼠体重、血象等生理指标与对照组相比无显著差异，提示e-As_4S_4具有良好的生物安全性。

结论：本研究通过热熔挤出技术制备了雄黄纳米颗粒，提高了雄黄的生物利用度，并在此基础上揭示了雄黄诱导白血病细胞分化的新功能和新机理，提示雄黄可作为分化诱导剂用于白血病治疗。

关键词：雄黄，纳米制剂，髓系白血病，分化

S12-7/12-4(16:30-16:45)

A new polysaccharide platform constructs self-adjuvant nanovaccines to enhance immune responses

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Nanovaccines have shown the promising potential in controlling and eradicating the threat of infectious diseases worldwide. There has been a great need in developing a versatile strategy to conveniently construct diverse types of nanovaccines and induce potent immune responses. To that end, it is critical for obtaining a potent self-adjuvant platform to assemble with different types of antigens into nanovaccines.

Here, we identified a new natural polysaccharide from the rhizomes of Bletilla striata (PRBS), and used this polysaccharide as a platform to construct diverse types of nanovaccines with potent self-adjuvant property. In the construction process of SARS-CoV-2 nanovaccine, PRBS molecules and RBD protein antigens were assembled into ~300 nm nanoparticles by hydrogen bond. For HIV nanovaccine, hydrophobic effect dominantly drove the co-assembly between PRBS molecules and Env expression plasmid into ~350 nm nanospheres. Importantly, PRBS can potently activate the behaviors and functions of multiple immune cells such as macrophages, B cells and dendritic cells. Depending on PRBS-mediated immune activation, these self-adjuvant nanovaccines can elicit significantly stronger antigen-specific antibody and cellular responses in vivo, in comparison with their corresponding traditional vaccine forms. Moreover, we also revealed the construction models of PRBS-based nanovaccines by analyzing multiple assembly parameters such as bond energy, bond length and interaction sites.

In conclusion, PRBS, a newly-identified natural polysaccharide which can co-assemble with different types of antigens and activate multiple critical immune cells, has presented a great potential as a versatile platform to develop potent self-adjuvant nanovaccines.

S6-1/12-4(13:30-13:50）

Single-chromosome Yeast Models Reveal the Configuration Robustness of Functional Eukaryotic Genomes

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Chromosomes in eukaryote nucleus carry genes, and are responsible for passing genetic information from parents to offspring. Different organisms usually contain different numbers of chromosomes. Whether the organization and/or number of chromosomes that have evolved in a particular species contribute to speciation reamins unclear. Here we have successfully established several single-chromosome fission yeast Schizosaccharomyces pombe models, in which the natural three chromosomes have been fused into one chromosome in different orders after deletion of the corresponding telomeres and centromeres. We have characterized the single-chromosome S. pombe cells in terms of morphology, growth, meiosis, genotoxic-drug sensitivity, chromosome structure, transcriptome and etc. Our results reveal the configuration robustness of eukaryotic genomes that can tolerate dramatic chromosome alterations.

S6-2/12-4(13:50-14:10）

基因、环境与长寿

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S6-3/12-4(14:10-14:30）

Transcriptomic insights into the longevity factors in centenarians

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S6-4/12-4(14:30-14:50）

Heterochronic parabiosis induces stem cell revitalization and systemic rejuvenation across aged tissues

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S6-5/12-4(14:50-15:10）

mRNA surveillance in mammalian ageing

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Nonsense-mediated mRNA decay (NMD) is a highly conserved post-transcriptional gene regulation mechanism. NMD degrades transcripts containing premature termination codons (PTCs) generated by genetic mutations, transcription errors or alternative splicing events, thus prevents the production of C-term truncated proteins insides a cell. Furthermore, NMD targets 3%-10% of a cellular transcriptome to regulate the abundance of physiological important RNA species. In humans, NMD is implicated in multiple diseases, including neurodevelopmental disorders (NDDs), autoimmune diseases and tumors. We recently generated a conditional knockout mouse line of NMD core factor Smg6 (the Smg6-PIN$^{flox/flox}$ mouse). By crossing the Smg6-PIN$^{flox/flox}$ mouse with the Nestin-Cre transgenic line, we found that loss of Smg6 in developing neocortex compromises neural stem cell self-renewal and promotes its premature differentiation. Consequently, Smg6 deficiency results in microcephaly and perinatal lethality in mice. Furthermore, we generated a Smg6 inducible deletion mouse line (Smg6-PIN$^{flox/flox}$ Cre-ER^{T2+}), and found loss of Smg6-NMD in adult mice causes early onset of ageing phenotypes through disturbing tissue homeostasis in major organs, including testis, intestine, and hematopoietic system. Our studies disclose essential roles of NMD in mammalian development and ageing.

Keywords: Nonsense-mediated mRNA decay; Development; Ageing; Mouse models

S6-6/12-4(15:10-15:25）

Structure of the human Meckel-Gruber protein Meckelin

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Mutations in the *Meckelin* gene account for most cases of Meckel-Gruber syndrome, the most severe ciliopathy with a 100% mortality rate. Here, we report a 3.3 Å cryo-electron microscopy structure of human Meckelin. The structure reveals a unique protein fold consisting of an unusual cysteine-rich domain that folds as an arch bridge stabilized by eleven pairs of disulfide bonds, a previously uncharacterized domain named β-sheet-rich domain, a novel seven-transmembrane fold wherein TM4-6 are broken near the cytoplasmic surface of the membrane, and a coiled-coil domain placed below the transmembrane domain. Meckelin forms a stable homodimer with an extensive dimer interface. Our structure establishes a framework for dissecting the function and disease mechanisms of Meckelin.

S6-7/12-4(15:25-15:40）

Sequestration of cellular native factors by protein aggregates

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Protein misfolding and aggregation are a hallmark of several neurodegenerative diseases (NDs), such as Huntington's disease (HD) and amyotrophic lateral sclerosis (ALS). However, how protein aggregation leads to cytotoxicity and neurodegeneration is still contentious. Accumulating evidence demonstrates that sequestration of cellular-interacting partners by protein aggregates contributes to the pathogenesis of these diseases. According to the interaction modes, we classified the sequestration effects into four types: protein co-aggregation, domain or motif-mediated sequestration, RNA-assisted sequestration, and sequestration of molecular chaperones. Thus, the cellular essential proteins and/or RNA hijacked by protein aggregates may lose their biological functions, thereby resulting in cytotoxicity and neurodegeneration. We have taken polyglutamine (polyQ) and RNA-binding proteins as models to investigate the mechanism underlying protein sequestration and its cellular impact. This presentation summarizes our recent progresses in sequestration of cellular native factors by protein aggregates and discusses the potential consequences to cellular availability, function, homeostasis, and proteinopathy.

Keywords: Protein aggregation; Sequestration; Interaction; Cellular homeostasis; Proteinopathy.

S6-8/12-4(15:40-15:55）

PINK1 regulates Aβ and hyperphosphorylated tau induced mitophagy-lysosomal degradation, neuroinflammation, and oxidative stress

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PTEN-induced putative kinase 1 (PINK1)/parkin mediates mitophagy, which is a specialized form of autophagy. To our knowledge, the contribution of PINK1 in Aβ and hyperphosphorylated tau-induced mitophagy-lysosomal degradation have not been fully and systematically reported. In the present study, we found that PINK1 knockout decreased the motor and cognitive function of 8 and 12-month-old SD rats, promoted mitochondrial fusion in the hippocampus of 4-month-old rats, and mitochondrial fission of 8 and 12-month-old rats, but inhibited mitochondrial fusion. Then, we used 4-month-old SD rats and PINK1-knockout SD rats to mimic two AD rat models by intracerebroventricular (ICV) microinjection of Aβ25-35 or forskolin (FSK, a PKA activator). We found that the expressions of mitophagy-related receptor proteins, LC3 and autophagy substrate p62/SQSTM1 in the hippocampus of ICV-Aβ rats were increased, while the expression of VAMP7 involved in autophagosome-lysosome fusion was decreased, and the mitophagy-lysosome pathway was blocked. Although PINK1 deficiency inhibited Aβ-induced increase in mitophagosomes, it aggravated lysosomal dysfunction, resulting in decreased mitophagosomes and autophagy substrate degradation, and ultimately aggravated the blockade of mitophagy-lysosomal pathway. The results of western blot, transmission electron microscopy, and immunofluorescence, all confirmed that PINK1 deficiency promoted Aβ-induced mitochondrial fusion. neuroinflammation, synaptic damage, and finally aggravated cognitive dysfunction in rats. Similar results were found in the hyperphosphorylated tau rat model, which was induced by ICV-FSK. PINK1 deficiency exacerbates FSK-induced tau pathology, synaptic damage, mitochondrial dysfunction and antioxidant system defects. Next, we used AAV-mediated gene interference technology to over-expressed PINK1 by injecting AAV into the tail vein of the SD rats. PINK1 over-expression inhibited Aβ and hyperphosphorylated tau-induced abnormal mitochondrial dynamics, alleviated neuroinflammation, synaptic damage and oxidative stress by activating PINK1/Parkin-mediated mitophagy-lysosomal pathway. Above all, our data support a critical role of PINK1-mediated mitophagy in controlling Aβ toxicity, mitochondrial quality, neuroinflammation, tau hyperphosphorylation and oxidative stress in AD.

S6-9/12-4(15:55-16:10）

Chaperone codes of Hsp70: from cysteine modifications to covalent inhibitors

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Hsp70 proteins are a family of ancient and conserved chaperones. They play important roles in vital processes, such as protein quality control and response to stress. Hsp70 proteins are drug targets for certain diseases, in particular cancer. Human HspA1A (hHsp70) contains five Cys residues, three in the nucleotide binding domain (NBD) and two in the substrate binding domain (SBD). Our previous studies have shown that the two Cys residues in the SBD are reactive under physiologically relevant oxidative conditions and glutathionylation of these residues modulates the structure and function of hHsp70. PES has been identified as an inhibitor of Hsp70 for over a decade. We found that PES can covalently bind to the α-helical bundle of the SBD (SBDα) of hHsp70 and causes similar structural and functional changes in hHsp70 as observed with glutathionylation. However our further study based on click-reaction-assisted activity-based protein profiling (click-reaction ABPP) indicated that PES could have multiple cellular protein targets. Development of specific covalent inhibitors targeting Hsp70 is still big challenge. To accumulate the basic information for it we also carefully explored the cysteine reactivity of hHsp70 and human HspA8 (hHsc70), and found the domain interaction and structural dynamics contribute to their different cysteine reactivity. These results facilitate understanding of the effects of redox and electrophiles on the chaperone activity and regulation mechanisms of Hsp70 proteins, and how these differences allow them to undertake distinct cellular roles.

Keywords: cysteine modifications, covalent inhibitors, Hsp70, cysteine reactivity

Reference (# co-first author, * corespondence author)

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S6-10/12-4(16:10-16:25)

CHK1 Controls Zygote Pronuclear Envelope Breakdown by Regulating F-actin through Interacting with MICAL3

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Mammalian zygote pronuclear envelope breakdown is an important guarantee for the successful initiation of first mitosis, but its regulatory mechanism remains largely unknown. Our previous study has identified CHK1 mutation could cause zygote arrest at pronuclei stage by affecting cell-cycle progress. However, the specific molecular mechanism on CHK1 modulating pronuclear envelope breakdown in zygotes needs to be further elucidated. In the current study, by transferring the pre-pronuclei from CHK1-mutation zygotes into the cytoplasm of normal enucleated fertilized eggs, we could successfully rescue mutation-caused zygote arrest and harvest high-quality blastocysts, which indicates that CHK1 dysfunction may tremendously destroy biological events mainly in the cytoplasm. We then found that CHK1 mutants affected the F-actin meshwork to disturb pronuclear envelope breakdown. By collecting 6000 mouse zygotes for Co-immunoprecipitation/Mass spectrum, we further identified that CHK1 interacted with MICAL3, a vital regulator of F-actin disassembly. While CHK1 mutants enhanced the interaction with MICAL3 and thus increased MICAL3 enzyme activity, resulting in excessive F-actin depolymerization. This study supplies an interpretation for the regulatory mechanism of pronuclear envelope breakdown during the transition from meiosis to the first mitosis in mammalian.

S15-1/12-4(13:30-13:50）

扫描电镜三维重建技术在细胞结构分析的应用

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脑连接组学通过绘制微观层面的大脑线路图来解析大脑的工作原理。具体来说，大脑线路图由神经元通过复杂的突触连接构成。神经元编码、处理和存储信息从根本上依赖于突触的连接模式以及在此基础之上的协调活动。突触的异常还与很多疾病有关，比如自闭症和阿尔兹海默症。因此，解析突触的亚细胞结构对理解大脑的结构与功能至关重要。随着大规模电子显微镜成像技术的快速发展，数据获取能力已经不再是制约大范围亚细胞结构重建的关键因素，但是自动分析方法和处理能力仍然滞后。目前，基于深度学习的突触亚细胞结构自动重建及可视化已成为目前的研究重点。本项工作首先构建了一套完整的突触三维结构和连接模式的自动识别、分析和可视化的工具集，并将其应用到突触的学习记忆模型，疾病模型以及小鼠耳蜗带状突触的识别与分析上，揭示了神经突触在实现精细功能调控的结构性证据。

S15-2/12-4(13:50-14:10)

Illumination of RNA dynamics using fluorescent RNAs

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Numerous studies show that RNAs have highly complex distributions, behaviors, and functions in cells. A robust fluorescent protein (FP)-like approach for tagging RNAs in order to monitor RNA dynamics in live cells remains to be developed. Here, we describe the development of two series of monomeric, highly bright, and stable fluorescent RNAs (FRs) with a broad range of emission maxima spanning from cyan to red. These FRs allow simple and robust imaging of mRNA and other RNA species in live cells with minimal perturbation of the target RNA's transcription, localization, and translation. We further show the usefulness of these FRs in imaging of genomic loci through CRISPR display, real-time tracking of protein-RNA tethering, and super-resolution imaging of RNA by structured illumination microscopy. These FRs provide ideal tools for live imaging of cellular RNAs.

S15-3/12-4(14:10-14:30）

耦合分子振动光谱的新型活细胞荧光成像技术

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荧光发射和拉曼散射都被广泛地用细胞传感和成像。荧光光谱技术可轻松实现单分子灵敏度。然而，常温下电子跃迁较宽的谱线限制了荧光光谱的化学特异性。相比之下，拉曼散射提供了关于分子结构、动力学和与环境耦合的精细化学信息。但拉曼散射本质上极其微弱，其散射截面比荧光分子的吸收截面小许多数量级。本报告将介绍一种新型混合光谱技术——受激拉曼激发荧光（SREF）。SREF光谱结合了拉曼光谱的高化学特异性和荧光光谱的高灵敏度，是目前唯一可以实现全远场单分子拉曼光谱成像的新型光谱成像技术。本报告将围绕SREF技术的发展，介绍其在细胞内电场传感成像，超分辨振动光谱成像，以及多色显微成像上的最新成果，并讨论其在活细胞成像与传感上的潜力。

S15-4/12-4(14:30-14:45)

DeepContact: High throughput quantification of membrane contact site based on electron microscopy imaging

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Membrane contact site (MCS)-mediated organelle interactions plays essential roles in the cell. Quantitative analysis of the MCS reveals vital clues for cellular responses under various physiological and pathological conditions. However, an efficient tool is lacking. Here, we developed “DeepContact”, a deep learning protocol for optimizing organelle segmentation and contact analysis based on label-free electron microscopy (EM). DeepContact presents high efficiency and flexibility in interactive visualizations, accommodating new morphologies of organelles and recognizing contacts in versatile width ranges, which enables statistical analysis of various types of MCSs in multiple systems. DeepContact profiled previously unidentified coordinative rearrangements of MCS types in cultured cells with combined nutritional conditioning. DeepContact also unveiled a subtle wave of ER-mitochondrial entanglement in Sertoli cells during the seminiferous epithelial cycle, indicating its potential in bridging MCS dynamics to physiological and pathological processes.

S15-5/12-4(14:45-14:55）

Seeing Is Solving -- Stunning Details in Living Cells Using Evident SIM-ultimate

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Live cell super-resolution imaging is now a growing application trend in life science, clinical research, and regenerative medicine studies. However, there is always a trade-off between spatial resolution, temporal resolution, and phototoxicity, making it a significant challenge to investigate fine structural dynamics in cells. We have developed both hardware and software solutions to overcome these challenges.

In this session, I will discuss how Evident's SIM-ultimate system, combines speed, sensitivity, and resolution for live-cell-compatible super resolution imaging. I will also be presenting several application examples where the Evident SIM-ultimate system has been effective.

* EVIDENT Is a wholly owned subsidiary of Olympus comprised of its former life science and industrial divisions. For over 100 years, Olympus has established itself as a leading innovator and manufacturer of excellent optical lenses and light microscopes. As of April, Olympus Scientific Solutions Division was reorganized into a separate company. The new company are now called Evident.

S15-6/12-4(14:55-15:05）

Leica’s latest advances in CLEM technology

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Electron microscopy is the most commonly used method to study the ultrastructure of cells and tissues in biology. Leica CLEM technology combines light and electron microscope sample preparation modes, enabling functional research to be located in the biological structure, discovering rapid and rare events in cell activities, and providing a powerful tool for life science research. This report will introduce the latest progress of Leica in the field of room temperature and cryogenics, bringing new power to scientific research.

S15-8/12-4(15:05-15:25）

单分子干涉定位成像技术及应用

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超分辨成像技术打破了光学衍射极限，促进了纳米尺度的原位生物学研究和精确定量分析，为阐述生物过程分子机制与探究疾病发生基础提供有力的技术手段。然而，许多细胞生物学问题需要在全细胞内同时对多个目标进行标记和纳米量级的三维成像。因此，我们搭建了基于双镜头架构的4Pi-SMS系统，通过荧光干涉提高系统的三维分辨率和成像深度；同时，利用几乎在所有荧光显微镜上都存在但被浪费的荧光信号，开发了一种新型的多色成像技术（Salvaged Fluorescence）；最后，进一步将两个技术结合起来，搭建了基于单光子干涉的多色三维超分辨率荧光显微镜，在全细胞内实现了三维各向同性10-15纳米的分辨率。我们利用该系统清楚解析了细胞内多种细胞器的超微结构与相互作用。该系统将成为解决重要细胞生物学问题有力工具。

S15-9/12-4(15:25-15:45）

活细胞代谢监测示踪与生命健康

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S15-10/12-4(15:45-16:00)

Solvatochromic biosensor reveals conformational changes of single molecules in living cells

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Revealing the activity or conformation while following the diffusion of individual proteins inside living cells is challenging, demanding biosensors that are sensitive, easy to deploy, and versatile. GTPases are switch-like enzymes that interact with downstream effectors only when they are in their GTP-bound conformation. We have developed biosensors for GTPase activity based on environment-sensing fluorescent dyes, purposefully using dyes that undergo spectral changes suitable for ratiometric imaging in living cells. For simple construction of biosensors within cells, we used membrane-permeable dyes that attach to the SNAP-tag incorporated in the biosensors. The SNAP/dye was positioned in a linker between the GTPase and a peptide that binds specifically to the active conformation of the GTPase. Through optimization, both Cdc42 and Rac1 biosensors showed a 25 nm shift in emission upon activation, along with a significant fluorescence lifetime increase.

Use of a single dye enabled ratiometric imaging without the need for bleach correction, greatly facilitating quantitative imaging. The biosensors (named SNAPsn Cdc42/Rac1) were sensitive because they were directly excited (in contrast to the indirect excitation of FRET). Single-molecule spectrum imaging and ratiometric imaging allow us to follow the spectra shift of individual molecules. Finally, we quantitatively mapped single Cdc42 molecule recruitment and activity across the cell, particularly around cell edge. We also studied the mechanism of nanoscale Cdc42 clusters in regulating its activity and determined the activation kinetics of Cdc42 at single molecule levels. Interestingly, we revealed the ultra-fast activity twinkling phenomenon of membrane-associated Cdc42, suggesting new insights into GTPases cycling.

S9-1/12-4(13:35-14:00）

纳米材料用于药物递送和免疫调节

闵元增

中国科学技术大学

S9-2/12-4(14:00-14:25）

KSHV and dilated Cardiomyopathy

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S9-3/12-4(14:25-14:50）

定量代谢组学与精准医学

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S9-4/12-4(15:15-15:40）

基于多元孟德尔随机化构建糖脂类性状的因果互作网络

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S9-5/12-4(15:40-16:05）

蛋白质组技术在临床中的应用

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S9-6/12-4(16:05-16:30）

Large-scale genomic data analyses reveal novel loci associated with phenotypic variation and genetic disease in humans

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