The 11th Biennial Meeting of Society for Free Radical Research-Asia
Chinese National Conference of Redox Biology and Medicine 2024
第11届亚洲自由基研究国际会议暨2024中国氧化还原生物学与医学大会

SFRR-Asia 2024

October 21-23, 2024, Beijing

Organizers:
Society for Redox Biology and Medicine Branch of Biophysical Society of China (SFRR-China)
中国生物物理学会氧化还原生物学与医学分会
School of Chinese Medicine, The University of Hong Kong
香港大学中医药学院

Co-organizers:
The Material Biology and Intelligent Medicine Branch of Biophysical Society of China
中国生物物理学会材料生物学与智能诊疗技术分会
Shanghai Tissuebank Biotechnology Co.,Ltd
上海荻硕贝肯生物科技有限公司

www.SFRR-Asia2024.com.cn

保健食品
国食健注 J20120011
国家市场监督管理总局批准

同仁堂牌
破壁灵芝孢子粉胶囊

浙江龙泉 | 道地药材 | 赤芝菌种

- 98%以上破壁率
- 香港GMP认证工厂生产

- 保健功能：本品经动物实验评价，具有增强免疫力的保健功能。
- 适宜人群：免疫力低下者。
- 不适宜人群：少年儿童、孕妇、乳母。
- 本品不能代替药品，适宜人群外的人群不推荐食用本产品。

注册号：国食健注J 20120011

同仁堂牌
破壁灵芝孢子粉胶囊

- 海藻囊材
- 香港制造

龙泉灵芝获得国家地理标志产品保护

生产商：
北京同仁堂国药有限公司
地址：新界大埔工业邨大景街3号　垂询电话：00852-36575819

炮製雖繁必不敢省人工
品味雖貴必不敢減物力

京食健广审（文）第241029-00159号

Contents / 目录

Welcome Message

Dear colleagues and friends:

On behalf of the organizing committee, I am honored to welcome you to "The 11th Biennial Meeting of the Society for Free Radical Research-Asia (SFRR-Asia) and the Chinese National Conference of Redox Biology and Medicine 2024" that will be held in Beijing, China from Oct. 21 to 23, 2024.

After two decades of ten past SFRR-Asia biennial meetings, we are marching into a new era to explore redox biology and medicine at precision, mechanistic and in vivo levels with innovative technology and multiple discipline collaborations. The SFRR-Asia 2024 with the theme "The new era of precision redox biology and medicine: from basic research to intervention of aging and diseases" will provide a great opportunity to address the updates on state-of-the-art research in these research fields. There will be a broad spectrum of topics concerning three aspects: Basic research on redox biology and medicine, Redox homeostasis in aging and diseases, Precision redox intervention and health management. For the first time, a special session entitled "Redox Future Perspective Forum" will be set aiming to draw the road map for future redox biology and medicine through open discussion with world-renowned leading scientists and experts. It's also exciting that Young Investigator Award (YIA) and Outstanding Poster/Oral Presentation Awards will be selected.

I sincerely welcome you to join the meeting and hope every participant will benefit from it in exchanging ideas, stimulating collaboration, developing friendship, and experiencing Chinese culture. We gratefully acknowledge the financial support from the SFRR-International, SFRR-Asia, and many sponsors listed in the program book and the conference website (SFRR-Asia2024.com.cn). I would like to thank all previous SFRR-Asia Biennial meeting organizers, Presidents and Secretariats for their outstanding contribution, dedication, and service to our society. My appreciation is extended to the Biophysical Society of China, the conference company and all volunteers for their cooperation and dedication. Finally, I cordially thank all SFRR-China council members and young investigators for their long-term strong support and solidarity.

I hope that the 11th SFRR-Asia will be a remarkable start for the next two decades!

Chang Chen

Chang Chen, PhD
President, SFRR-China
President-Elect, SFRR-Asia

About SFRR-Asia

The Society for Free Radical Research (Asian Region), founded in 1995, is an Asian regional branch of the Society for Free Radical Research International (SFRRI).

Current Officers of SFRR-Asia

President

Young-Joon Surh (Seoul National University, Korea)

President-Elect

Chang Chen (Chinese Academy of Sciences, China)

Secretary-General

Osamu Handa (Kawasaki Medical School, Japan)

Treasurer

Hidehiko Nakagawa (Nagoya City University, Japan)

Representatives

Shinya Toyokuni (Graduate School of Medicine, Nagoya University, Japan)
Noriko Noguchi (Toshisha University, Japan)

Past Presidents

1st: Toshikazu Yoshikawa (Japan)
2nd: Myung-Hee Chung (Korea)
3rd: Toshihiko Ozawa (Japan)
4th: Baolu Zhao (China)
5th: T. Paul A. Devasagayam (India)
6th: Kalanithi Nesaretnam (Malaysia)
7th: Jeen-Woo Park (Korea)
8th: Daniel Tsun-Yee Chiu (Taiwan, China)
9th: Shinya Toyokuni (Japan)
10th: Yang Liu (China)
11th: Yuji Naito (Japan)

Previous Biennial Meetings

The 1st SFRR-Asia Biennial Meeting

Date: November 6-8, 2003

Venue: Cultural Center of Seoul National University, Seoul, South Korea

Organizer: Myung-Hee Chung

The 2nd SFRR-Asia Biennial Meeting

Date: June 24-29, 2005

Venue: Galaxy Hotel, Shanghai, China

Organizer: Baolu Zhao

The 3rd SFRR-Asia Biennial Meeting: Emerging Trends in Free Radical and Antioxidant Research

Date: January 8-11, 2007

Venue: Fariyas Holiday Resort, Lonavala, India

Organizer: R.D. Lele

The 4th SFRR-Asia Biennial Meeting: Chemoprevention and Translational Research

(In conjunction with the 7th COSTAM/SFRR International Workshop)

Date: July 9-12, 2009

Venue: Langkawi Island, Malaysia

Organizer: Kalanithi Nesaretnam

The 5th SFRR-Asia Biennial Meeting

(In conjunction with the 8th Conference of Asian Society for Mitochondrial Research & Medicine and 11th Conference of Japanese Society of Mitochondrial and Medicine)

Date: August 31-September 4, 2011

Venue: Kagoshima Citizens' Culture Hall, Kagoshima, Japan

Organizer: Hideyaki Majima

The 6th SFRR-Asia Biennial Meeting: Oxidative Stress and Mitochondrial Alterations in Ageing and Disease

Date: October 16-19, 2013

Venue: The Second Medicine Building, Chang Gung University, Tao-Yuan, Taiwan, China

Organizer: Daniel Tsun-Yee Chiu

The 7th SFRR-Asia Biennial Meeting: Advanced Oxidative Stress Research for Health and Well-beings

Date: November 29-December 2, 2015

Venue: The Empress Hotel, Chiang Mai, Thailand

Organizers: Maitree Suttajit & Malyn Ungsurungsie

The 8th SFRR-Asia Biennial Meeting: Cross Talk between Free Radicals and Mitochondria in Health and Disease

(In conjunction with the 14th Conference of the Asian Society of Mitochondrial Research & Medicine and Chinese Mitochondrial Society 2017)

Date: September 8-11, 2017

Venue: Xi'an Nanyang Hotel, Xi'an, China

Organizer: Jiangkang Liu

Co-chairs: Yang Liu, Chin-San Liu, and Quan Chen

The 9th SFRR-Asia Biennial Meeting

Date: April 4-7, 2019

Venue: Kyoto International Community House (Kokoka), Kyoto, Japan

Organizer: Yuji Naito

The 10th SFRR-Asia Biennial Meeting: New Paradigm for Research on Oxidative Stress & Inflammation

Date: November 4-6, 2022

Venue: Center for New Drug Development, Seoul National University main campus (Gwanak), Seoul, Korea

Organizer: Young-Joon Surh

The 11th SFRR-Asia Biennial Meeting: New Research Horizons for Redox Biology and Medicine

(In conjunction with Chinese National Conference of Redox Biology and Medicine 2024)

Date: October 21-23, 2024

Venue: Kun Tai Hotel Beijing Wangjing, Beijing, China

Organizer: Chang Chen

Sponsor: Society for Redox Biology and Medicine (Branch of Biophysical Society of China)

Co-sponsor: The Material Biology and Intelligent Medicine (Branch of Biophysical Society of China)

International Organizing Committee

Chaiyavat Chaiyasut (Chiang Mai University, Thailand)

Chalermpong Saenjum (Chiang Mai University, Thailand)

Chang Chen (Chinese Academy of Sciences, China)

Hidehiko Nakagawa (Nagoya City University, Japan)

Jin-Won Hyun (Jeju National University, Korea)

Kalanithi Nesaretnam (Malaysia)

Ke Jian "Jim" Liu (Stony Brook University, USA)

Liang-Jun Yan (The University of North Texas, USA)

Malyn Ungsurungsie (Silpakorn University, Thailand)

Osamu Handa (Kawasaki Medical School, Japan)

Pingsheng Liu (Chinese Academy of Sciences, China)

Salmaan Hussain (Petroliam Nasional Berhad, Malaysia)

Shinya Toyokuni (Nagoya University, Japan)

Subrata. Chattopadhyay (Bhabha Atomic Research Center, India)

Tsong-Long Hwang (Chang Gung University, Taiwan, China)

Xin Gen Lei (Cornell University, USA)

Yong Ji (Harbin Medical University, China)

Yongping Bao (University of East Anglia, UK)

Young-Joon Surh (Seoul National University, Korea)

Yuji Naito (Kyoto Prefectural University of Medicine, Japan)

Yun-Sil Lee (Ewha Womans University, Korea)

Zigang Dong (Zhengzhou University, China)

International Advisory Committee

Baolu Zhao (Chinese Academy of Science, China)

Daniel Tsun-Yee Chiu (Taiwan, China)

Giovanni E. Mann (King's College London, UK)

Helmut Sies (Heinrich-Heine-Universität Düsseldorf, Germany)

Junji Yodoi (Kyoto University, Japan)

Maitree Suttajit (University of Phayao, Thailand)

Myung-Hee Chung (Gachon University, Korea)

Raekil Park (GIST, Korea)

Shanlin Liu (Fudan University, China)

T. Paul A. Devasagayam (India)

Toshikazu Yoshikawa (Japan)

Yang Liu (Chinese Academy of Sciences, China)

Yau-Huei Wei (Mackay Medical College, Taiwan, China)

Local Organizing Committee

Conference Chair

Chang Chen (Institute of Biophysics, Chinese Academy of Sciences, China)

Co-Chairs

Jiangang Shen (The University of Hong Kong, China)

Huiyong Yin (City University of Hong Kong, China)

Jian-Ping Cai (Beijing Hospital, China)

Yan-Zhong Chang (Hebei Normal University, China)

JianKang Liu (University of Health and Rehabilitation Sciences, Xi'an Jiaotong University, China)

Secretary-General

Guangjun Nie (National Center for Nanoscience and Technology, China)

Secretariat

Yuanyuan Wang (Institute of Biophysics, CAS, China)
Libo Du (Institute of Chemistry, CAS, China)
Wanxia Jiao (Biophysical Society of China)
Hai Wu (Beijing Huaweizhongyi Technology Co., Ltd.)
Jin Meng (Capital Medical University, China)
Fangyuan Li (Shanghai Jiao Tong University, China)

Local scientific committee

Yan An	Xiuping Chen	Jianzhang Huang	Xingguo Liu	Jun Lu
Zhongbing Lu	Qiang Liu	Jin Meng	Anuo Nan	Pingping Shen
Dongyun Shi	Huiru Tang	Ye Tian	Taotao Wei	Jie Zhang
Qiang Zhao	Yuming Zhao	Bo Zhou	Chenggang Zou	Qiang Zou

Organizing committee

Qinghui Ai	Liangzhao Chu	Guozhen Cui	Cuixia Di
Wenjun Ding	Libo Du	Zhihui Feng	Yinbin Feng
Zhonghong Gao	Lee Jia	Jinlian Li	Simon Ming-Yuen LEE
Ping Li	Wenli Li	Yang (泱) Li	Yang (洋) Li
Bin Liu	Ke Liu	Yangping Liu	Yanlin Ma
Yulan Qiu	Moshi Song	Bo Tang	Jun Wang
Suhua Wang	Hai Wu	Jianqiang Xu	Li Xu
Xianquan Zhan	Hong Zhang	Yan Zhao	Zhongzheng Zhen
Li Zhong			

General Information

Conference Date

From 8:30 AM on Oct. 21 (Monday) to 22:00 PM on Oct. 23 (Wednesday), 2024.

Registration Open

Registration desk is located at the lobby of Kuntai Hotel and open during the following hours:

Oct. 20 (Sunday) 09:00-21:00;

Oct. 21 (Monday) to Oct. 23 (Wednesday): 8:00-18:00;

Group Photo Session

Date & Time: Oct. 21 (Monday) 10:00-10:20

Venue: The Ballroom

Name Badge

Participants are requested to wear their name badges during all scientific programs and social events. The conference staffs have the right to refuse entry to any session without the proper name badge.

Conference Policy

Please switch your mobile phone off or to the vibration mode in the conference room.

No photography and recording lectures or posters are allowed.

Internet Access

Free wireless internet service will be available in the conference venue. Ask the staff in the registration desk for the login information.

Official Language

The official language of the conference is English.

Weather

The average temperature in Beijing during the conference periods is about 9-19℃

Electricity

P.R.C operates on a 220V supply voltage and 50Hz.

Refreshments & Boxed Lunches

Beverages and light snacks will be provided during the coffee breaks and poster presentation session.

Boxed lunches will be provided for the registered participants.

Social Events

Welcome Reception (All registered participants are invited)

Date & Time: 18:30-20:00 on Oct. 21(Monday)

Venue: The Ballroom, Kuntai Hotel

Gala Dinner (By invitation Only)

Date & Time: 18:00-22:00 on Oct. 22 (Tuesday)

Venue: Hua's Restaurant (Dong Zhi Men)

Address: No.5 Dongzhimen Inner Street, Dongcheng Strict, Beijing.

Banquet:

Closing & Award Ceremony (All registered participants are invited)

Date & Time: 18:00-22:00 on Oct. 23 (Wednesday)

Venue: The Ballroom, Kuntai Hotel

Conference Venue

Kuntai Hotel (Beijing Wangjing)

Phone: (86-10) 84106666

Fax: (86-10) 84106688

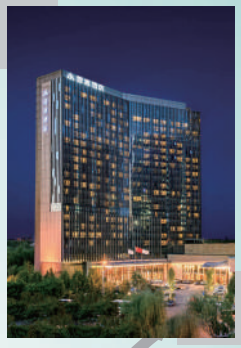
Website: http://www.kuntaihotel.com

Address: No 2, Qiyang Road, Chaoyang District, Beijing

Zip code: 100102

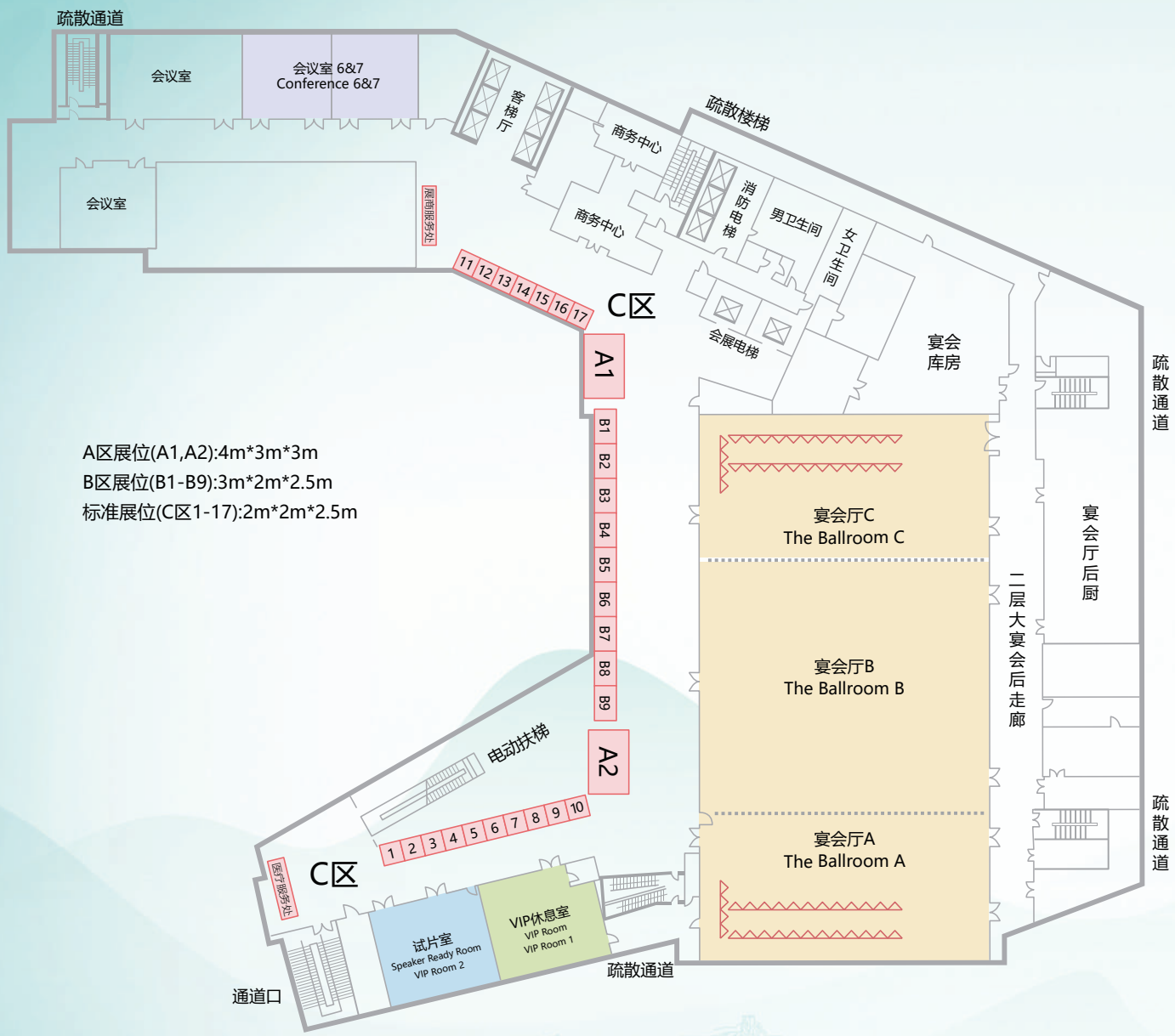
Email: Public@kuntaihotel.com

Map:



North Fifth Ring Road
Wangjing Station
Kuntai Hotel
(Beijing Wangjing)
Subway Line 13
Subway Line 15
Jingmi Road
Airport Expressway
North Fourth Ring Road
Subway Line 10
Subway Line 14

Conference venue floor plan & exhibition booth distribution map



A区展位(A1,A2):4m*3m*3m
B区展位(B1-B9):3m*2m*2.5m
标准展位(C区1-17):2m*2m*2.5m

Sponsors

A区展位

A1 北京同仁堂国药有限公司

Beijing Tong Ren Tang Chinese Medicine Company Limited

A2 上海荻硕贝肯生物科技有限公司

Shanghai Tissuebank Biotechnology Co.,Ltd

B区展位

B1 上海皓元生物医药科技有限公司（MCE 中国）

MedChemExpress

B2 武汉爱博泰克生物科技有限公司

ABclonal Technology Co.,Ltd.

B3 江苏集萃药康生物科技股份有限公司

GemPharmatech Co., Ltd

B4 励德爱思唯尔信息技术（北京）有限公司

Reed Elsevier Information Technology (Beijing) Co., Ltd

B5 北京华威中仪科技有限公司

Beijing Huawei Zhongyi Technology Co., Ltd

B6 MDPI

B7 《逆境生物学（英文）》编辑部

Editorial Office of Stress Biology

B8 上海漙美医疗科技有限公司

Asclepius Meditec Co., Ltd.

B9 上海碧云天生物技术股份有限公司

Beyotime Biotech Inc

C区展位

C1 仪景通光学科技（上海）有限公司
EVIDENT (Shanghai) Co., Ltd.

C2 上海拜谱生物科技有限公司
Shanghai Bioprofile Technology Co., Ltd

C3 山东安然纳米实业发展有限公司
Shandong Anran Nanometer Industry Development Co., Ltd

C4 日本生物压力研究振典速合
Japan Biostress Research Promotion Alliance (JBPA)

C5 北京隆福佳生物科技有限公司
Beijing Longfujia Biological Technology Co., Ltd

C6 杭州华安生物技术有限公司
HUABIO

C7 北京科爱森蓝文化传播有限公司
KeAi Communications Co., Ltd

C8 布鲁克（北京）科技有限公司
Bruker (Beijing) Technology Co., Ltd

C9 上海阔云仪器设备有限公司
Shanghai Kuo Yun Instruments Co., Ltd

C10 世界精密仪器商贸（上海）有限公司
World Precision Instruments

C11 北京晟乾鑫源科技发展有限公司
Beijing Sheng Qian Xin Yuan Science and Technology Development Co., Ltd

C12 喀斯玛（北京）科技有限公司
CASmart (Beijing) Technology Co., Ltd

C13 上海怡赛科学仪器有限公司
Shanghai E-SCI Scientific Instrument Co., Ltd

C14 仕润生物科技（山东）有限公司
Shirun Biotechnology (Shandong) Co., Ltd

C15 山东高歌医疗器械有限公司
Shandong Gaoge Medical Equipment Co., Ltd

C16 江苏瑞明生物科技有限公司
Jiangsu Rayme Biotechnology Co., Ltd

C17 北京中海联盛科贸有限公司
Beijing Zhonghai Liansheng Science and Trade Co., Ltd

其他赞助

康诺生物制药股份有限公司
Knature Biopharmaceutical Co.,Ltd.
香港平安堂藥業有限公司
PINGAN TANG PHARM (HK) LIMITED
北京普利莱基因技术有限公司
BEIJING APPLYGEN TECHNOLOGIES CO.,LTD.
JBKLAB（South Korea）

Timetable

Oct. 20, 2024 Sunday	
Open for Registration	**Open for Registration** Lobby of Kuntai Hotel 09:00-21:00 Oct. 20 08:00-18:00 Oct. 21 08:00-18:00 Oct. 22 08:00-18:00 Oct. 23

Date & Time	Day1 Oct. 21, 2024 Monday			Date & Time	Day2 Oct. 22, 2024 Tuesday			Date & Time	Day3 Oct. 23, 2024 Wednesday		
08:30-09:00	**Opening Ceremony** The Ballroom										
09:00-09:30	**Plenary Lecture-1 (PL-1)** The Ballroom			09:00-09:30	**Plenary Lecture-3 (PL-3)** The Ballroom			09:00-09:30	**Symposium-13 (S13)** The Ballroom A	**Symposium-14 (S14)** The Ballroom B	**Symposium-15 (S15)** The Ballroom C
09:30-10:00	**Plenary Lecture-2 (PL-2)** The Ballroom			09:30-10:00	**Special Lecture** The Ballroom			09:30-10:00			
10:00-10:20	**Group Photo** The Ballroom **Coffee Break** Poster Hall			10:00-10:20	**Coffee Break** Poster Hall			10:00-10:20	**Coffee Break** Poster Hall		
10:20-12:00	**Symposium-1 (S1)** The Ballroom A	**Symposium-2 (S2)** The Ballroom B	**Symposium-3 (S3)** The Ballroom C	10:20-12:00	**Symposium-7 (S7)** The Ballroom A	**Symposium-8 (S8)** The Ballroom B	**Symposium-9 (S9)** The Ballroom C	10:20-12:00	**Flash Talk-1 (FT-1)** The Ballroom A	**Flash Talk-2 (FT-2)** The Ballroom B	**Flash Talk-3 (FT-3)** The Ballroom C
12:00-12:30	**12:00-13:30 SFRR-Asia Business Meeting** Conference 2-6&7 on the second floor of Kuntai Hotel	**Lunch** The Ballroom		12:00-12:30	**Lunch** The Ballroom			12:00-12:30	**12:00-13:30 SFRR-China Business Meeting** Conference 2-6&7 on the second floor of Kuntai Hotel	**Lunch** The Ballroom	
12:30-13:30		**Poster Presentation** The Ballroom A		12:30-13:30	**Meet the Editors** The Ballroom			12:30-13:30		**Poster Presentation** The Ballroom C	
13:30-15:10	**Symposium-4 (S4)** The Ballroom A	**Symposium-5 (S5)** The Ballroom B	**Symposium-6 (S6)** The Ballroom C	13:30-15:10	**Symposium-10 (S10)** The Ballroom A	**Symposium-11 (S11)** The Ballroom B	**Symposium-12 (S12)** The Ballroom C	13:30-14:00	**Plenary Lecture-4 (PL-4)** The Ballroom		
								14:00-14:30	**Plenary Lecture-5 (PL-5)** The Ballroom		
								14:30-14:50	**Coffee Break** Poster Hall		
15:10-15:30	**Coffee Break** Poster Hall			15:10-15:30	**Coffee Break** Poster Hall			14:50-17:00	**Redox Future Perspective Forum** The Ballroom		
15:30-17:30	**Symposium-YIO-1 (Y-1)** The Ballroom A	**Symposium-YIO-2 (Y-2)** The Ballroom B	**Symposium-YIO-3 (Y-3)** The Ballroom C	15:30-17:30	**Symposium-YIO-4 (Y-4)** The Ballroom A	**Symposium-YIO-5 (Y-5)** The Ballroom B	**Symposium-YIO-6 (Y-6)** The Ballroom C				
17:30-18:30	**Exhibition Sharing Session** The Ballroom C			18:00-22:00	**Gala dinner (invited only)**			17:00-18:00	**Exhibition Exchange** Exhibition Area		
18:30-20:00	**Welcome Reception** The Ballroom							18:00-22:00	**Closing & Award Ceremony Banquet** The Ballroom		
20:00-22:00	**Early Career Researchers** The Ballroom C										

Scientific Program

08:30-09:00	**Opening Ceremony**	The Ballroom
Chair: Gunangjun Nie 聂广军 (National Center for Nanoscience and Technology, China)		
	Plenary Lecture -1 (PL-1)	The Ballroom
Chair: Chang Chen 陈畅 (Institute of Biophysics, CAS, China)		
09:00-09:30	Giovanni E Mann (King's College London, UK)	
	Roadblock for clinical translation: importance of physiological oxygen levels for high throughput screening of redox	
	Plenary Lecture -2 (PL-2)	The Ballroom
Chair: Malyn Ungsurungsie (Silpakorn University, Thailand)		
09:30-10:00	Young-Joon Surh (Seoul National University, Korea)	
	Warburg Effect Revisited: Role of NRF2 in Pseudohypoxic Stabilization of HIF-1α	
10:00-10:20	**Group Photo** **Coffee Break**	The Ballroom Poster Hall
	Symposium-1 (S1) **Redox signaling in organelles/cell fate/development/reproduction**	The Ballroom A
Chair: Taotao Wei 卫涛涛 (Institute of Biophysics, CAS, China) Hun Taeg Chung (Daegu Haany University, Korea)		
10:20-10:40	Ming-Yi Bai 白明义 (Shandong University, China)	
	H_2O_2 promotes stomatal development and opening through regulating SnRK1	

Oct. 21

10:40-11:00	Wenhua Zheng 郑文华 (University of MacauUniversity of Macau, China)
	Artemisinin attenuates astrocyte overactivation by inhibiting IRE1 phosphorylation and the downstream NF-κB pathway in Alzheimer's disease
11:00-11:20	Takaaki Akaike (Tohoku University, Japan)
	Redox Signal Regulation by Supersulfides
11:20-11:40	Hun Taeg Chung (Daegu Haany University, Korea)
	Carbon monoxide sensitizes cancer cell to erastin-induced ferroptosis via ROS-PERK-ATF4
11:40-12:00	Erich Gnaiger (Beijing Huawei Zhongyi Technology Co. Ltd)
	Oxidative phosphorylation, H_2O_2 production, mitochondrial membrane potential, coenzyme Q redox state, and calcium uptake: from tissue normoxia to deep hypoxia

Symposium-2 (S2)
Redox and aging①"Targeting Redox and Mitochondria to delay aging and prevent age-related diseases"Forum — The Ballroom B

Chair: Ke Liu 刘科 (Sichuan University, China)
Malcolm Jackson (The University of Liverpool, UK)

10:20-10:40	Min-Xin Guan 管敏鑫 (Zhejiang University, China)
	Vitamin A treatment rescues retinal cell-specific deficiencies caused by Leber's hereditary optic neuropathy-linked mtDNA mutation
10:40-11:00	Yuguang Shi 史裕光 (Barshop Aging Institute, UT-Health, San Antonio)
	Cardiolipin Remodeling byALCAT1 Controls the Mitochondrial Free Radical Clock
11:00-11:20	Zhiyin Song 宋质银 (Huazhong University of Science and Technology, China)
	A new mode of mitochondria-lysosome contacts under hypoxia
11:20-11:40	Yidong Bai (University of Texas Health San Antonio, USA)
	Mitochondrial electron transfer chain (ETC) in aging and longevity

11:40-12:00	Malcolm Jackson (The University of Liverpool, UK)
	Dysregulation of hydrogen peroxide-mediated responses to contractile activity in skeletal muscle loss associated with ageing

Symposium-3 (S3) **Redox and obesity, vascular function and metabolism**	The Ballroom C
Chair: Zhongbing Lu 陆忠兵 (University of Chinese Academy of Sciences, China) Juan Sastre (University of Valencia, Spain)	
10:20-10:40	Xiao-Wei Chen 陈晓伟 (Peking University, China)
	ER oxi-lipidosis drives MASH pathogenesis
10:40-11:00	Changtao Jiang 姜长涛 (Peking University, China)
	Gut microbial enzymes: new targets for intervention in metabolic diseases
11:00-11:20	Junli Liu 刘军力 (Shanghai Jiao Tong University, China)
	Obstructive sleep apnea syndrome and hepatic lipid metabolism disorders
11:20-11:40	Juan Sastre (University of Valencia, Spain)
	Redox signaling in acute inflammation
11:40-12:00	Michael Jonathan Davies (University of Copenhagen, Denmark)
	Oxidation and enzyme-mediated changes to the artery wall in cardiovascular disease

12:00-13:30	**SFRR-Asia Business Meeting** Lunch Provited	Conference 2-6&7 on the second floor of Kuntai Hotel
12:00-12:30	**Lunch**	The Ballroom

12:30-13:30	**Poster Presentation**	The Ballroom A

	Symposium-4 (S4) **New approach for precision redox research**	The Ballroom A
	Chair:Xiangliang Yang 杨祥良 (Huazhong University of Science and Technology, China) Kwang Pyo Kim (Kyung Hee University, Korea)	
13:30-13:50	Bo Tang 唐波 (Laoshan Laboratory, China)	
	Fluorescence Imaging for the Progression of Oxidative Stress-Related Diseases	
13:50-14:10	Yonggang Yao 姚永刚 (Kunming Institute of Zoology, CAS, China)	
	Primate Phenotype and Genetic Analyses – From Basic Research to Clinical Applications	
14:10-14:30	Huiru Tang 唐惠儒 (Fudan University, China)	
	Quantitative metabolomics for redox biology and medicine	
14:30-14:50	Youjun Yang 杨有军 (East China University of Science and Technology, China)	
	Near-infrared xanthene dyes and *in vivo* ROS sensing	
14:50-15:10	Young-Sam Keum (Dongguk University, Korea)	
	Leucine 305 and 309 residues contribute to the formation of two human NRF2 bands in SDS-PAGE	

	Symposium-5 (S5) **Discovery of new molecules in redox network**	The Ballroom B
	Chair: Qiang Zhao 赵强 (Nankai University, China) Ken-ichi Yamada (Kyushu University, Japan)	
13:30-13:50	Jingbo Pi 皮静波 (China Medical University, China)	
	NRF1 and NRF2 coordinate osteoclastogenesis and bone remodeling via ROS-dependent and independent mechanisms	

13:50-14:10	Akira Nakai (Yamaguchi University Graduate School of Medicine, Japan)
	HSF1 regulates nuclear/cytoplasmic and mitochondrial proteotoxic stress responses
14:10-14:30	Bo Xie 谢波 (Shanghai Tissuebank Biotechnology Co.,Ltd (TAB))
	Grasip the void of Redox——the new relic of Tissue Bank
14:30-14:50	Ken-ichi Yamada (Kyushu University, Japan)
	Structural library and visualization of endogenously oxidized lipids
14:50-15:10	Youngjoo Kwon (Ewha Womans University, Korea)
	Regulation of protein-protein interactions as a new paradigm in drug discovery: Targeting the oncogenic role of E74 Like ETS transcription factor 3 (ELF3) through modulation of its protein protein interaction

Symposium-6 (S6)
Redox modification of biomacromolecules
The Ballroom C

Chair: Zhonghong Gao 高中洪 (Huazhong University of Science and Technology, China)
Koji Uchida (The University of Tokyo, Japan)

13:30-13:50	Lee Jia 贾力 (Minjiang University, China)
	Biology and pharmaceutical development of S-nitrosylation
13:50-14:10	Huiyong Yin 尹慧勇 (City University of Hong Kong, China)
	Lipid Peroxidation and Cardiovascular Disease
14:10-14:30	Moran Benhar (Technion Israel Institute of Technology, Israel)
	The dynamic thiol redox proteome of macrophages and its role in the response to oxidative-inflammatory stress
14:30-14:50	Koji Uchida (The University of Tokyo, Japan)
	Immune memory against toxic aldehydes

14:50-15:10	Xingen Lei (Cornell University, USA)
	A protein protein interaction between SOD1 and YWHAZ and YWHAE

15:10-15:30	**Coffee Break**	Poster Hall

	Symposium-YIO-1 (Y-1) **Redox modification of biomacromolecules** **Redox and obesity, vascular function and metabolism**	The Ballroom A
	Chair: Li Xu 徐力 (Jilin University, China) Hyoung Kyu Kim (Inje University, Korea)	
15:30-15:45	Lei Chen 陈雷 (Peking University, China)	
	Activation mechanism of phagocyte NADPH oxidase	
15:45-16:00	Xueqing Ba 巴雪青 (Northeast Normal University, China)	
	OGG1 promotes iTreg differentiation and alleviates mouse IBD by facilitating Foxp3 transcriptional activation	
16:00-16:15	Ming Lu 鲁明 (Shanghai Institute of Nutrition and Health, CAS, China)	
	A lactate-lipid peroxidation-acetate metabolic axis between tumor-associated macrophages and cancer cells fuels hepatocellular carcinoma metastasis	
16:15-16:30	Shi Yuheng 石玉衡 (Fudan university, China)	
	STING: A Potential Target for Suppressing the Development of Clonal Hematopoiesis and Leukemia	
16:30-16:45	Wen Wang 王雯 (Capital Medical University, China)	
	Disorder of nitration/S-sulfhydration participates in hyperhomocysteinemia progression and liver damage	
16:45-17:00	Bin Liu 刘斌 (Shantou University, China)	
	Endothelium-dependent contraction, NO and cardiovascular disorders in the absence of prostacyclin synthesis	

17:00-17:15	Hou-Zao Chen 陈厚早 (Chinese Academy of Medical Sciences & Peking Union Medical College, China)
	SIRT2 governs a cytoplasm-mitochondrial signal to repress mitochondrial ROS and vascular ageing
17:15-17:30	Hyoung Kyu Kim (Inje University, Korea)
	Tetrahydrobiopterin is a Promising Target of Diabetic Cardiomyopathy via Restoring Mitochondria Function

Symposium-YIO-2 (Y-2)
Redox and cancer, infection and immunity
Redox and environmental challenge
The Ballroom B

Chair: Jianghong Man 满江红 (National Center of Biomedical Analysis, China)
Chung S. Yang (Rutgers, The State University of New Jersey, USA)

15:30-15:45	Jianqiang Xu 许建强 (Dalian University of Technology, China)
	Two sesquiterpene lactones inhibit TXNRD1 and induce endoplasmic reticulum stress in cancer cells
15:45-16:00	Xiu-Ping Chen 陈修平 (University of Macau, China)
	Novel anticancer drug discovery strategies by targeting NQO1
16:00-16:15	Kelong Fan 范克龙 (Institute of Biophysics, CAS, China)
	Structure-Activity Relationship and Biomedical Applications of Nanozymes
16:15-16:30	Cui-xia Di 狄翠霞 (Institute of Modern Physics, CAS, China)
	Electron FLASH Irradiation Ameliorates Radiation-induced Developmental and Neurological Toxicity in Zebrafish Model
16:30-16:45	Tomohiro Sawa (Kumamoto University, Japan)
	Supersulfide regulation of innate immune responses
16:45-17:00	Tianli Zhang (Akita University, Japan)
	Supersulfides regulate NLRP3 inflammasome activation through sensing homeostasis

17:00-17:15	Guoping Yin 尹国平 (Beijing Tsinghua Changgung Hospital, China)
	OSA induced multiple-system damage via oxidative stress
17:15-17:30	Jian-gang Long 龙建纲 (Xi'an Jiaotong University, China)
	HTHB: A Potential Therapeutic Agent for Cognitive Impairment and Inflammation

Symposium-YIO-3 (Y-3) Redox and neural function and mental health	The Ballroom C
Chair: Wenli Li李文丽 (Air Force Medical University, China) Changyang Gong 巩长旸 (Sichuan University, China)	
15:30-15:45	Jun Wang 王军 (Hubei University of Technology, China)
	Redox biomarkers for prognosis of infectious diseases
15:45-16:00	Yuming Zhao 肇玉明 (Capital Medical University, China)
	DDAH1, a key neuroprotective player, promotes neurogenesis and neural repair after cerebral ischemia insults
16:00-16:15	Danqian Liu 刘丹倩 (Institute of Neuroscience, CAS, China)
	A physiological role of H_2O_2 in sleep homeostasis
16:15-16:30	Ishii Tetsuro (University of Tsukuba, Japan)
	NRF2 translocation from dendrites to nucleus in glutamatergic pyramidal neurons induced by uncoupling of post-synaptic neuronal nitric oxide synthase via calcium influx through NMDAR
16:30-16:45	Meiling Wu 吴美玲 (The University of Hong Kong, China)
	Peroxynitrite reduces Treg cell expansion and function by mediating IL-2R nitration and aggravates multiple sclerosis pathogenesis
16:45-17:00	Xianhua Wang 王显花 (Peking University, China)
	ROMO1 shields the mitochondrial cysteinome from oxidations in diseases and aging

17:00-17:15	Xu Zhang 张栩 (Tianjin Medical University, China) Alox15/15-HpETE Aggravates Myocardial Ischemia-Reperfusion Injury by Promoting Cardiomyocyte Ferroptosis
17:15-17:30	Yan Zheng 郑焱 (The First Affiliated Hospital of Xi'an Jiaotong University, China) The Mechanisms of Plasma-Activated Solutions in Treating Atopic Dermatitis

17:30-18:30	**Exhibition Sharing Session**	The Ballroom C

18:30-20:00	**Welcome Reception**	The Ballroom

Chair: Jian Kang Liu 刘健康 (University of Health and Rehabilitation Sciences/Xi'an Jiaotong University, China)

20:00-22:00	**Early Career Researcher**	The Ballroom C

	Plenary Lecture-3 (PL-3)	The Ballroom
	Chair: Myung-Hee Chung (Seoul National University, Korea)	
09:00-09:30	Yuji Naito (Kyoto Prefectural University of Medicine, Japan)	
	Gut frailty: its concept and the role of dietary fiber	
	Special Lecture	The Ballroom
	Chair: Yang Liu 刘扬 (Institute of Chemistry, CAS, China)	
09:30-10:00	Chang Chen 陈畅 (Institute of Biophysics, CAS, China)	
	Carry forward the cause and forge ahead into the future —— Memory of past 20 years SFRR-Asia biennial meetings	
10:00-10:20	**Coffee Break**	Poster Hall
	Symposium-7 (S7) **Redox signaling in organelles/cell fate/development/reproduction**	The Ballroom A
	Chair: Dongyun Shi 施冬云 (Shanghai Medical College of Fudan University,Shanghai, China) Francisco Rafael Martins Laurindo (University of São Paulo, Brazil)	
10:20-10:40	Wenjun Ding 丁文军 (University of Chinese Academy of Sciences, China)	
	Airborne PM2.5-induced oxidative stress aggravates neurotoxicity in olfactory bulb	
10:40-11:00	Yanlin Ma 马燕琳 (The First Affiliated Hospital of Hainan Medical College, China)	
	Deciphering Umbilical Cord Blood Hematopoietic Stem/Progenitor Cell Alterations in Alpha-Thalassemia Using Single-Cell Transcriptomics	
11:00-11:20	Liron Bar-Peled (Harvard Medical School Department of Medicine, USA)	
	Identification of Druggable and Redox Vulnerabilities in Cancer	

11:20-11:40	Francisco Rafael Martins Laurindo (University of São Paulo, Brazil)
	An endoplasmic reticulum-based model of intercellular redox communication.
11:40-12:00	Kyung-Soo Chun (Keimyung University, Korea)
	Apoptotic Effect of Terfenadine, a Histamine H1 Receptor Antagonist, and Terfenadine-loaded Human Serum Albumin Nanoparticles in Colorectal Cancer and Glioblastoma Cells

Symposium-8 (S8)
Redox and aging ②"Targeting Redox and Mitochondria to delay aging and prevent age-related diseases"Forum — The Ballroom B

Chair: Young Zhang 张勇 (Tianjin University of Sport, Tianjin, China)
Liang-Jun Yan (University of North Texas Health Science Center, Fort Worth, TX, USA)

10:20-10:40	Han-Ming Shen 沈汉明 (University of Macau, China)
	Redox regulation of mitophagy by targeting PINK1
10:40-11:00	Xingguo Liu 刘兴国 (Guangzhou Biomedicine and Health Institute, CAS, China)
	NAD^+ dependent UPRmt activation underlies intestinal aging caused by mitochondrial DNA mutations
11:00-11:20	Quan Chen 陈佺 (Institute of Zoology, Chinese Academy of Sciences, China)
	Truncated oxidized phospholipids mediate synchronized ferroptosis and contribute to acute kidney injury
11:20-11:40	Liang-Jun Yan (University of North Texas Health Science Center, Fort Worth, TX, USA)
	NAD^+-dependent enzymes in health and disease: Our key findings on NADH-ubiquinone oxidoreductase in diabetic pancreas
11:40-11:55	Kanglin Wang 王康林 (Knature Bio-pharma Co., Ltd.)
	Mitochondrial drug NAD^+ anti-aging strategy

	Symposium-9 (S9) **Redox and cancer, infection and immunity**	The Ballroom C
	Chair: Pingping Shen 沈萍萍 (Nanjing University, China) Junji Yodoi (Kyoto University, Japan)	
10:20-10:40	Zigang Dong 董子钢 (Zhengzhou University, China)	
	The role of redox metabolism in drug resistance of cancer therapy	
10:40-11:00	Yoshiro Saito (Tohoku University, Japan)	
	Redox biology regulated by selenoproteins- significance for biological defense and its relation to cancer	
11:00-11:20	Martin Rottenberg (Karolinska Institutet, Sweden)	
	Immune Mechanisms and Oxidative Stress Underlying the Interaction of Tuberculosis and Diabetes	
11:20-11:40	Junji Yodoi (Kyoto University, Japan)	
	TRX Thioredoxin redox regulator of inflammasome: Redoxisome Concept	
11:40-12:00	Mee-Hyun Lee (Dongshin University, Korea)	
	A Systemic Effects of Herbal Medicine on Colon Diseases	
12:00-12:30	**Lunch**	The Ballroom
12:30-13:30	**Meet the Editors**	The Ballroom
	Chair: Huiyong Yin 尹慧勇 (City University of Hong Kong, China)	

Symposium-10 (S10) Redox and environmental challenge	The Ballroom A
Chair: Libo Du 杜立波 (Institute of Chemistry, CAS, China) Jin-Won Hyun (Jeju National University, Korea)	
13:30-13:50	Yinghui Li 李莹辉 (China Astronaut Research and Training Center, China)
	Research progress and thinking of space medicine omics
13:50-14:10	Qi Xie 谢旗 (Institute of Genetics and Developmental Biology, CAS, China)
	Gγ regulates PIP2 phosphorylation in ROS distribution to affect crop tolerant to alkaline stress
14:10-14:30	Jin-Won Hyun (Jeju National University, Korea)
	Particulate matter and reactive oxygen species
14:30-14:50	Jung-Hwan Kim (Gyeongsang National University, Korea)
	TCDD-induced Lysosomal SLC46A3 modulates hepatic cytosolic copper homeostasis resulting in triglyceride accumulation
14:50-15:10	Dae Young Kwon (Korea Food Research Institute, Korea)
	Redox History of Earth, and Life of Organisms and Foods Crops

Symposium-11 (S11) Traditional Medicine Prophylaxis-Therapeutics and Redox Balance (Sponsored by The University of Hong Kong & Beijing Tong Ren Tang Chinese Medicine Co. Ltd.)	The Ballroom B
Chair: Simon Ming-Yuen LEE 李铭源 (The Hong Kong Polytechnic University, Hong Kong, China) Motohiro Nishida (Kyushu University, Japan)	
13:30-13:50	Jing-yan Han 韩晶岩 (Peking University, China)
	Traditional Chinese medicine ameliorates cardiac and cerebral microvascular injury through regulating mitochondrial respiratory chain

Oct. 22

13:50-14:10	Jiangang Shen 沈剑刚 (The University of Hong Kong, China)
	Niuhuang Qingxin Wan is a promising anti-depressive agent to attenuate chronic stress induced depressive- and anxiety-like behaviors through promoting hippocampal neurogenesis and modulating TrkB/ERK/CREB signaling pathway
14:10-14:30	Xinli Li 李新立 (The First Affiliated Hospital of Nanjing Medical University, China)
	Qiliqiangxin in the Treatment of Heart Failure with Reduced Ejection Fraction ------ Research Progress
14:30-14:50	Motohiro Nishida (Kyushu University, Japan)
	Cardiac stress resistance regulated by sulfur metabolism
14:50-15:10	Yibin Feng 冯奕斌 (The University of Hong Kong, China)
	The role of oxidative stress and antioxidants in liver disease therapy

Oct. 22

Symposium-12 (S12) The Ballroom C

Natural products and nutrition in anti-aging and health management

(Sponsored by The University of Hong Kong & Beijing Tong Ren Tang Chinese Medicine Co. Ltd.)

Chair: Bo Zhou 周波 (Lanzhou University, China)
Ae-son Om (Hanyang university, Korea)

13:30-13:50	Lina Qu 曲丽娜 (China Astronaut Research and Training Center, China)
	Research on Space Biological Rhythm Intervention Strategies Based on Redox Regulation
13:50-14:10	Qinghui Ai 艾庆辉 (Ocean University of China, China)
	Phosphatidylethanolamine alleviates OX-LDL-induced macrophage inflammation by upregulating autophagy and inhibiting NLRP1 inflammasome activation
14:10-14:30	Andrew Bulmer (Griffith University, Australia)
	Translation of bilirubin's redox potential to preventative and therapeutic medicine – use of models, and the development of therapies

14:30-14:50	Hye-Kyung Na (Sungshin Women's University, Korea) A Catechol Isoquinoline Salsolinol Induces Cell Death of Human Liver Cancer Cells by Regulating the STAT1/3 Signaling
14:50-15:10	Yun-Sil Lee (Ewha Womans University, Korea) From Target Identification to Early-Stage Therapeutic Discovery: Leveraging In Vivo Preclinical Models

15:10-15:30	**Coffee Break**	Poster Hall

Symposium-YIO-4 (Y-4)
New approach for precision redox research
Intelligence materials for precision redox intervention

The Ballroom A

Chair: Xianquan Zhan 詹显全 (Cancer Hospital and Institute, Shandong First Medical University, China)
Kenji Sato (Kyoto University, Japan)

15:30-15:45	Ling Fu 付玲 (Academy of Military Medical Sciences, China) Chemical proteomics reveals mechanisms of bacterial response to ROS mediated by antibiotics
15:45-16:00	Yuan Guo 郭媛 (Northwest University, China) Molecule-Guided Precise Identification and Intervention of Senescence
16:00-16:15	Yangping Liu 刘阳平 (Tianjin Medical University, China) Simultaneous Quantitation of Persulfides, Biothiols and Hydrogen Sulfide through Efficient Sulfur Exchange Reaction with Trityl Spin Probes
16:15-16:30	Ai-Hui Tang 唐爱辉 (University of Science and Technology of China, China) Spatial Transcriptome Profiling of a Huntington's Disease Mouse Brain with BASSFISH

16:30-16:45	Kenji Sato (Kyoto University, Japan)
	Generation of short chain aldehydes and increase of oxidative stress in mice by intake of fructose
16:45-17:00	Yue Yuan 袁月 (University of Science and Technology of China, China)
	GSH-induced in situ peptide self-assembly for precise tumor imaging and ROS-based therapy
17:00-17:15	Yang Li 李洋 (Shenzhen Institute of Advanced Technology, CAS, China)
	Molecular targeting nano drug candidates
17:15-17:30	Lizeng Gao 高利增 (Institute of Biophysics, CAS, China)
	Nanozybiotics: Advancing Antimicrobial Strategies Through Biomimetic Mechanisms

Oct. 22

Symposium-YIO-5 (Y-5)
Discovery of new molecules in redox network
Natural products and nutrition in anti-aging and health management

The Ballroom B

Chair: Jun Lu 陆军 (Southwest University, China)
Ock Jin Park (Hanyang university, Korea)

15:30-15:45	Zhi-Yong Mao 毛志勇 (Tongji University, China)
	Targeting DNA repair to extend lifespan
15:45-16:00	Jinzhi Lu 鲁锦志 (The First Affiliated Hospital, Yangtze University, China)
	Redox-Regulated Iron Metabolism and Ferroptosis in Ovarian Cancer: Molecular Insights and Therapeutic Opportunities
16:00-16:15	Moshi Song 宋默识 (Institute of Zoology, CAS, China)
	Restored PGAM5-mediated Oxeiptosis Eliminates ROShigh Cardiomyocytes and Improves Cardiac Function during Cardiac Aging

16:15-16:30	Jin Li 李瑾 (Beijing Hospital, China)
	Exploring the Neuroinflammatory Pathways of 8-oxoGTP and Their Effects on Cognitive Decline
16:30-16:45	Jin Meng 孟劲 (Capital Medical University, China)
	ATF-4 and hydrogen sulfide signaling mediate longevity in response to inhibition of translation or mTORC1
16:45-17:00	Guozhen Cui 崔国祯 (Zunyi Medical University, China)
	Network Medicine landscape on the Health-Enhancing Properties of Natural Antioxidants
17:00-17:15	Jing Qu 曲静 (Institute of Zoology, CAS, China)
	Cellular Senescence and Rejuvenation
17:15-17:30	Chalermpong Saenjum (Chiangmai University, Thailand)
	A hybrid sweet potato (Maejo 341) mitigates LPS-induced inflammation and RANKL-induced osteoporosis by regulating ROS-mediated pathways

Oct. 22

Symposium-YIO-6 (Y-6) Redox signaling in organelles/cell fate/development/reproduction	The Ballroom C
Chair: Zhangjian Huang 黄张建 (China Pharmaceutical University, China) Youngtae Jeong (Daegu Gyeongbuk Institute of Science and Technology, Korea)	
15:30-15:45	Jie He 何杰 (Institute of Neuroscience, CAS, China)
	cxcl18b-defined transitional state-specific nitric oxide signaling drives injury-induced Müller Glia proliferation in the zebrafish retina
15:45-16:00	Peng Huang 黄鹏 (Shenzhen University, China)
	Transforming nutrition into reactive oxygen species for tumor treatment

16:00-16:15	Weihua Yu 于卫华 (The Fourth Military Medical University, China)
	Mitochondrial dynamics and redox balance control macrophage cell fate
16:15-16:30	Ye Tian 田烨 (Institute of Genetics and Developmental Biology, CAS, China)
	Mitochondrial Superoxide Stress Response: Implications for Aging and Health
16:30-16:45	Lei Wang 王磊 (Institute of Biophysics, CAS, China)
	The ER redoxtasis: from basic research to the intervention of aging and diseases
16:45-17:00	Chao Li 李超 (East China Normal University, China)
	Regulation of plant development by peptides–receptor kinases–ROS signaling
17:00-17:15	Youngtae Jeong (Daegu Gyeongbuk Institute of Science and Technology, Korea)
	Reciprocal role of the Keap1-Nrf2 pathway in the self-renewal and differentiation of airway stem cells and tongue stem cells
17:15-17:30	Yong Yeon Cho (Catholic University, Korea)
	Involvement of UVB/ROS-mediated signaling pathway in karyoptotic cell death

18:00-22:00	**Gala dinner (invited only)** Meet at the lobby of Kuntai Hotel at 6 PM

Oct. 22

Symposium-13 (S13) Redox and neural function & mental health	The Ballroom A
Chair: Lin Mei 梅林 (Chinese Academy of Medical Sciences & Peking Union Medical College, China) Lin Mantell (St. John's University, USA)	
09:00-09:20	Chuanzhu Yan 焉传祝 (Qilu Hospital of Shandong University, China)
	Flavin adenine dinucleotide metabolism and related neuromuscular disorders
09:20-09:40	Ping Li 李平 (Shandong Normal University, China)
	In-situ Fluorescence Imaging of Brain Disease-associated Bioactive Molecules
09:40-10:00	Lin Mantell (St. John's University, USA)
	Mechanisms of α7 nicotinic acetylcholine receptor in modulating inflammatory lung injury and infection

Symposium-14 (S14) Intelligence materials for precision redox intervention	The Ballroom B
Chair: Fangyuan Li (Songjiang Hospital, Shanghai Jiao Tong University School of Medicine, China) Yong Sang Song (Seoul National University, Korea)	
09:00-09:20	Guangjun Nie 聂广军 (National Center for Nanoscience and Technology, China)
	Regulation and restoration of microenvironment homeostasis of intestinal diseases based on nanotechnology
09:20-09:40	Jun Zhou 周军 (Huazhong University of Science and Technology, China)
	Molecular mechanisms of selenium intervention in metabolic diseases through regulation of redox homeostasis
09:40-10:00	Yong Sang Song (Seoul National University, Korea)
	Next-generation RNA Sequencing-based Deep-learning Model to Predict Chemoresistance in High-grade Serous Ovarian Carcinoma

Symposium-15 (S15) Lifestyle and redox regulation	The Ballroom C
Chair: Cheng-Gang Zou 邹成钢 (Yunnan University, China) Osamu HANDA (Kawasaki Medical School, Japan)	

09:00-09:20	Tong-Jin Zhao 赵同金 (Fudan University, Shanghai, China)
	Surplus fatty acid synthesis increases oxidative stress in adipocytes and lnduces lipodystrophy
09:20-09:40	Hao Wu 吴昊 (Capital University of Physical Education and Sports, China)
	Effects of Hyperbaric Oxygen Intervention on Oxidative Stress in the Body after High-Intensity Interval Training
09:40-10:00	Osamu HANDA (Kawasaki Medical School, Japan)
	The role of ileal mucosa -associated microbiota in the patients with Crohn's disease

10:00-10:20	**Coffee Break**	Poster Hall

Oct. 23

	Flash Talk-1 (FT-1)	The Ballroom A
	Chair: Suhua Wang 王素华 (Guangdong University of Petrochemical Technology, China)	
10:20-10:25	Kishimoto Ayuta (Shibaura Institute of Technology, Japan)	
	Detection and evaluation of novel oxidizing substances in sodium hypochlorite using Trolox	
10:25-10:30	Ujihara Miyu (Kyoto University, Japan)	
	High sensitive LC-MS/MS method for determining malondialdehyde in biological sample using thiobarbituric derivatization	
10:30-10:35	Yan Wang 王炎 (Tianjin Medical University, China)	
	A Chelator-linked Trityl Probe Enabling Highly Specific, Sensitive and Quantitative Detection of Cu(I) by EPR Spectroscopy	
10:35-10:40	Wong Nai-Kei (Shantou University Medical College, China)	
	Deciphering the RSS code in cellular senescence	
10:40-10:45	Zhijuan Hu 胡志娟 (Guangzhou Institute of Biomedicine and Health, CAS, China)	
	A novel protein CYTB-187AA encoded by the mitochondrial gene CYTB modulates mammalian early development	

Chair: Ju Cui 崔菊 (Country Beijing Institute of Geriatrics, National Health Commission, China)

10:45-10:50	Zongmin Li 李宗敏 (Peking University First Hospital, China)
	Elucidating the reducibility of sulfur dioxide on cysteine proteomes
10:50-10:55	Mi Xinya (Kyushu University, Japan)
	TRPC6-mediated Zn^{2+} influx improves heart failure through supersulfide formation
10:55-11:00	Xinhua Qiao 乔新华 (Institute of Biophysics, CAS, China)
	Exploring the collaboration of redox and autophagy systems based on a genome-wide new redox genes screening
11:00-11:05	Chenlin Su (Kyushu University, Japan)
	TRPC6-mediated Zn^{2+} influx mitigates cardiac fibrosis through maintaining redox homeostasis
11:05-11:10	Jiao Meng 孟姣 (Institute of Biophysics, CAS, China)
	A novel redox gene atad-3 identified by whole genome RNAi screening in Caenorhabditis elegans

Chair: Chalermpong Saenjum (Chiangmai University, Thailand)

11:10-11:15	Yong Wang 王勇 (Ocean University of China, China)
	Ferrocene Correlates with Ferroptosis: Multiple Approaches to Explore Ferrocene-appended GPX4 Inhibitors as Anticancer Agents
11:15-11:20	Shuo Sun 孙硕 (Institute of Biophysics, CAS, China)
	Discovery of small molecule inhibitors specifically targeting the Ero1α-PDI oxidative protein folding pathway
11:20-11:25	Yongjie Zhang 张永杰 (China Pharmaceutical University, China)
	Unraveling the roles of Glutathione S-transferase P in protein S-glutathionylation modulation: Implications of therapeutic targets for oxidative organ injury
11:25-11:30	Jinwen Yang 杨劲文 (Huazhong University of Science and Technology, China)
	Detection of Protein Tyrosine Nitration or Amination
11:30-11:35	Siyu Tian 田丝雨 (Hebei Normal University, China)
	Brain-targeted liposomes with neuroprotective effects for precise therapy of ischemic stroke

11:35-11:40	Xi Hu 胡希 (Anhui University of Chinese Medicine, China)
	Nanomaterials for tumor-cell-specific catalytic therapy
11:40-11:45	Yingnan Liu 刘英楠 (University of Salzburg, Austria)
	Nano-assemblies overcome cancer multidrug resistance for effectively synergistic chemo-immuno-oncotherapy
11:45-11:50	Guofang Zhang 张国芳 (Shenzhen Institute of Advanced Technology, CAS, China)
	Nanomedicine by Modulating ROS for Oncotherapy
	Jing Mu 穆婧 (Peking University Shenzhen Hospital, China)
11:50-11:55	Protective effect of platinum nano-antioxidant and nitric oxide against hepatic ischemia-reperfusion injury
11:55-12:00	Xiaoyan Zhong 仲晓燕 (Soochow University, China)
	Scintillating nanodots as sonosensitizers for cancer sonodynamic therapy

Flash Talk-2 (FT-2) The Ballroom B

Chair: Yan An 安艳 (Soochow University, China)

10:20-10:25	Yuanyuan Wang 王圆圆 (Institute of Biophysics, CAS, China)
	Targeting the integrated stress response and redox balance is a new strategy in meningioma inhibiting
10:25-10:30	Jiabin Yu 于佳斌 (Jeju National University, Korea)
	Loss of poly(ADP-ribose) polymerase 1 promotes catalase activation via the endothelin receptor
10:30-10:35	Chaorui Guo 郭朝瑞 (China Pharmaceutical University, China)
	Myeloperoxidase (MPO) plays a key role in mitophagy in murine macrophages
10:35-10:40	Lili Xin 信丽丽 (Soochow University, China)
	PM2.5 induced iron accumulation-associated liver injury via activation of ferroptosis and NLRP3 inflammasome
10:40-10:45	Huaiwei Liu 刘怀伟 (Shandong University, China)
	Polysulfides mediate multiple types of protein modification and tumor growth

Chair: Jinchuan Hu 胡晋川 (Fudan University, China)

10:45-10:50	Zhongwei Zhao 赵仲伟 (Beijing University of Chemical Technology, China)
	Physiologically relevant Fenton-like reactions and redox cycles of labile iron species: implications for ferroptosis and Alzheimer's disease
10:50-10:55	Seino Anna (Shibaura Institute of Technology, Japan)
	The changes of genes and protein which affects mitochondrial fusion and fission in AD transgenic mice
10:55-11:00	Yingmin Zhang 张英敏 (Beijing Hospital, China)
	The molecular mechanism study of oxidized microRNA regulating P21 and promoting aging
11:00-11:05	Zhongda Li 李忠达 (Hebei Normal University, China)
	The Beneficial Effects of Knockout of Astrocytic Ceruloplasmin on Learning and Memory Function in Aging Mice
11:05-11:10	Lvtao Zeng 曾律滔 (Beijing Hospital, China)
	Analysis of aging biomarkers and construction of a physiological age prediction model based on cytokine profiling

Chair: Yan Zhao 赵燕 (Institution, Country Harbin Institute of Technology (Weihai), China)

11:10-11:15	Jing Wu 武婧 (Soochow University, China)
	PM2.5-induced premature senescence in HUVECs through the SIRT1/ PGC-1α/SIRT3 pathway
11:15-11:20	Dong He 何东 (Shantou University, China)
	Disruption of E-prostanoid 3 receptor on cardiomyocytes protects against heart ischemia reperfusion injury
11:20-11:25	Shanzhuang Niu 牛善壮 (Yunnan University, China)
	The molecular mechanism of lysosome function impairment and promotes fat accumulation by loss of G6PD
11:25-11:30	Cuomao Niangji 娘吉措毛 (Qinghai University Affiliated Hospital, China)
	Metabolic reprogramming in placental mitochondria respiration contributes to the reproductive success of indigenous Tibetan women living at high altitude
11:30-11:35	Xiaolin Tian 田晓琳 (Shanxi Medical University, China)
	Fecal microbe transplantation ameliorates arsenic-and-fluoride-induced nephrotoxicity of offspring rats co-exposure to arsenic and fluoride through microbiota-gut-kidney axis

Chair: Tomohiro Sawa (Kumamoto University, Japan)

11:35-11:40	Zhang Lu (The University of Hong Kong, China)
	Ganoderma Lucidum Spore Lehuo Powder Attenuates Experimental Autoimmune Encephalomyelitis by Modulating Microglial Activation and Polarization through the NF-κB Signaling Pathway
11:40-11:45	Bingping Yang 杨冰萍 (Shantou University Medical College, China)
	Disruption of circadian rhythms promotes ventricular arrhythmia via oxidative stress and electrocardiography alternation
11:45-11:50	Fei Zhou 周飞 (University of Macau, China)
	Chrysanthemolide J mitigates acetaminophen-induced hepatotoxicity through LKB1 and PP2A-mediated mitochondrial hormesis
11:50-11:55	Mengchen Liu 刘梦晨 (Zhuhai campus of Zunyi Medical University, China)
	Network Medicine landscape on the Health-Enhancing Properties of Natural Antioxidants

Oct. 23

Flash Talk-3 (FT-3) — The Ballroom C

Chair: Julia Li Zhong 钟莉 (Chongqing University, China)

10:20-10:25	Xu Zhang 张旭 (Zhengzhou University, China)
	Hydrogen Peroxide Turn on Heat as Thermogenic agents and signals: Cellular Thermoregulation in Physiologies and Pathphysiologies
10:25-10:30	Qianlei Yang 杨乾磊 (Soochow University, China)
	Redox regulated Mitophagy in Arsenite-induced Malignant Transformation of Human Keratinocytes
10:30-10:35	Chenghua Luo 罗成华 (Shihezi University, China)
	Endogenous hydrogen sulfide promotes the proliferation and metastasis of breast cancer through PGK1 S-sulfhydration
10:35-10:40	Jia Han 韩佳 (Kanazawa Medical University Hospital, Japan)
	High PRDX4 Expression Can Predict Worse Pathological Characteristics in Cutaneous Squamous Cell Carcinom
10:40-10:45	Jie Chen 陈杰 (Shanghai Jiao Tong University School of Medicine, China)
	Radix Rehmanniae and its Active Ingredients Ameliorate CFA-Induced Inflammation by Attenuating Macrophage-Mediated Localized Response and Nitrative Damage

Chair: Junmin Zhang 张军民 (Lanzhou University, China)

10:45-10:50	Pengfei Liu 刘朋飞 (The Second Affiliated Hospital of Xi 'an Jiaotong University, China)
	Pharmacological targeting of NRF2 represents a promising therapeutic approach for ferroptosis-related diseases
10:50-10:55	Qingyu Wang 王清宇 (Beijing Hospital, China)
	Increased oxidative stress induced by high-fat and high-fructose diets contribute to type 2 diabetes and its associated complications
10:55-11:00	Yau-Tuen Chan (The University of Hong Kong, China)
	Role of miR-3689a-3p in the regulation of mitochondrial oxidative stress in the sorafenib resistance of hepatocellular carcinoma
11:00-11:05	Guoquan Liu 刘国全 (Peking University Health Science Center, China)
	LPO-dependent lipid rafts inhibit immunogenic ferroptosis and pyroptosis in melanoma
11:05-11:10	Yusheng Lu 卢余盛 (Minjiang University, China)
	S-nitrosylation enhances RhoA activity and promotes tumor cell invasion and metastasis

Chair: Kuei-Hung Lai (Taipei Medical University, Taiwan, China)

11:10-11:15	Xize Li 李析泽 (University of Health and Rehabilitation Sciences, China)
	The circ_0071616-miR-140-3p-USP34 axis mediates FoxM1 deubiquitination in Helicobacter pylori-induced gastric malignant transformation
11:15-11:20	Tingxu Jin 金庭旭 (Soochow University, China)
	A Bayesian benchmark concentration analysis for urinary fluoride and intelligence in adults in Guizhou, China
11:20-11:25	Qiong Wu 吴琼 (Hebei Normal University, China)
	Circadian-Cognitive Synchrony Disrupted: Iron's Influence on Rhythmic and Memory-Related Neural Functions
11:25-11:30	Qianjin Liu 刘前进 (Xuzhou Medical University, China)
	Mechanism analysis of oxidative stress and inflammation in brain diseases
11:30-11:35	Lingyan Su 苏凌燕 (Yunnan Agricultural University, China)
	S-nitrosoglutathione reductase alleviates morphine analgesic tolerance by restricting PKCα S-nitrosation

11:35-11:40	Zhen Li 李振 (Shenzhen Hospital of Integrated Traditional Chinese and Western Medicine, China)
	Phase separation of BRD2 promotes ferritinophagy in depression
11:40-11:45	Xiaoli Zhang 张小莉 (Shanxi Medical University, China)
	Mechanism of arsenic regulation of mitochondrial damage and autophagy induced synaptic damage through SIRT1 and protective effect of melatonin
11:45-11:50	Treethip Sukkho (Chiang Mai University, Thailand)
	Osteoprotective and osteoblastic potential of the Sambucus javanica Reinw ex Blume subsp. javanica leave

12:00-13:30	**SFRR-China Business Meeting Lunch Provided**	Conference 2-6&7 on the second floor of Kuntai Hotel
12:00-12:30	**Lunch**	The Ballroom
12:30-13:30	**Poster Presentation**	The Ballroom C

Oct. 23

Plenary Lecture-4 (PL-4) — The Ballroom

Chair: Jian Kang Liu 刘健康 (University of Health and Rehabilitation Sciences/Xi'an Jiaotong University, China)

13:30-14:00	Rui-Ping Xiao 肖瑞平 (Peking University, China)
	Role of CaMKII in heart cell fate regulation

Plenary Lecture-5 (PL-5) — The Ballroom

Chair: Yan-Zhong Chang (Hebei Normal University, China)

14:00-14:30	Zu-Hang Sheng (National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health(NIH), USA)
	Energy Matters: Reprogramming of Redox Signaling and Mitochondrial Energy Metabolism in Aged Neurons

14:30-14:50	**Coffee Break**	Poster Hall

14:50-17:00	**Redox Future Perspective Forum** **——The road map for future redox biology and medicine**	The Ballroom

Topic 1, Redox is the basis of life and the common reason for diseases.
Topic 2, The main challenge of redox biology and medicine research in the future.
Topic 3, Advocating "International Redox-decode Project" with multidisciplinary global-level collaborations, in both basic and clinical research.

Chair: Rui-Ping Xiao 肖瑞平 (Peking University, China)

14:50-16:30	**Opening Message** (Video) from Prof. Helmut Sies, Heinrich-Heine-Universitat Düsseldorf, Germany **Panelist Discussion** Chang Chen, China / Andrew Bulmer, Australia / Francisco Laurindo, Brazil / Giovanni Mann, UK / Juan Sastre, Spain / Lin Mantell, USA / Malcolm Jackson, UK / Michael J Davies, Denmark / Xingen Lei, USA / Young-Joon Surh, Korea / Yuji Naito, Japan / Zu-Hang Sheng, USA
16:30-17:00	Open for Discussion

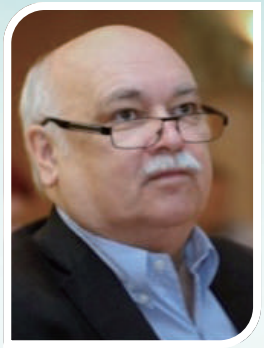
17:00-18:00	**Exhibition Exchange**	Exhibition Hall

18:00-22:00	**Closing & Award Ceremony & Banquet**	The Ballroom

Chair: Jiangang Shen 沈剑刚 (The University of Hong Kong, China)

Oct. 23

Plenary Lecture - 1(PL-1)



Roadblock for clinical translation: importance of physiological oxygen levels for high throughput screening of redox therapeutics in live cell models

Giovanni E. Mann

School of Cardiovascular and Metabolic Medicine & Sciences, King's British Heart Foundation Centre of Research Excellence, Faculty of Life Sciences & Medicine, King's College London, UK

Email: giovanni.mann@kcl.ac.uk

Abstract

In vivo, vascular and other cell types are exposed to physiological oxygen levels ranging from to ~2-13 kPa O_2, while cells cultured in standard CO_2 gassed incubators are routinely exposed to hyperoxic O_2 levels (18 kPa O_2). Although the importance of studying cellular redox signalling under physiological O_2 levels is established, few studies have examined the effects of long-term adaptation of cells to different O_2 levels (Keeley & Mann, Physiol. Reviews 2019;99:161-234; Sies et al., Nature Rev Mol. Cell Biol. 2022;23:499-515). As molecular mechanisms regulating NRF2 mediated redox signaling have primarily been studied under hyperoxia, we characterised NRF2 gene targets in endothelial cells following 5d adaptation to 18 kPa, physiological normoxia (5 kPa) or hypoxia (1 kPa) using O_2 regulated Scitive workstations. Activation of NRF2 and induction of GSH-related genes were insensitive to changes in pericellular O_2 levels, whereas induction of HO-1 and NQO1 in response to electrophiles or NO was attenuated under 5 kPa O_2 due to enhanced expression of the NRF2 repressor Bach1 (Chapple et al., FRBM 2016;92:152-62). Furthermore, a PP2A-mediated feedback mechanism regulates Ca^{2+}-dependent endothelial NO synthesis under 5 kPa O_2 (Keeley et al., FASEB J. 2017;31: 5172-5183), with NO bioavailability increased significantly in cells adapted to 5 kPa O_2 (Keeley et al., FASEB J. 2017;31: 5172-5183; Sevimli et al., Redox Biology 2022;53:1023190; Altun et al., Free Radic Biol Med., 2024;221:89-97). Notably, enhanced SERCA activity under 5 kPa O_2 protects endothelial cells against calcium overload (Keeley et al., FASEB J. 2018;32:2531-2538). We recently employed ICP-MS and LA-ICP-MS to measure changes in total metal content in human coronary artery endothelial (Redox Biol., 2023;62:102712) and smooth muscle (Redox Biol., 2023:64:102777) cells cultured long-term under hyperoxia (18 kPa), physiological normoxia (5 kPa) and hypoxia (1 kPa O_2) and then subjected to ischemia-reoxygenation. We are currently investigating metabolome and lipidome profiles and redox phenotype of human brain microvascular endothelial cells (hCMEC/D3) adapted long-term to 18 kPa or 5 kPa O_2 and laminar shear stress. In summary, adapting cell models in vitro to physiological O_2 levels enhances the physiological relevance of high throughput screening of therapeutics and drugs for clinical translation.

Key words: Redox Biology, KEAP1/NRF2, Reactive Oxygen Species, Physiological Oxygen

Short CV

Prof. Giovanni Mann obtained his BSc in Zoology (1973) from George Washington University, Washington D.C., USA and MSc (1974) and PhD in Physiology (1978) from University College London. He was subsequently appointed to a 4-year postdoctoral Research Fellowship at Queen Elizabeth College London and then to a Lectureship in Physiology (1981), Readership in Physiology (1992) and as Professor of Vascular Physiology (1997-) at King's College London. He is an Associate Editor for Physiological Reviews, Reviews and Special Issues Editor for Free Radical Biology & Medicine and Chair of the FRBM Ethics Committee, President of the Society of Free Radical Research-International (SFRRI), and previously served as President-Elect and General Secretary of SFRRI, Chairman of The Physiological Society, President of the British Microcirculation Society, President of the European Microcirculation Society, President of the Society for Free Radical Research-Europe and President of the European Pancreatic Society. He was elected as a Fellow of The Physiological Society in 2018. He has previously served on Editorial Boards of The Journal of Physiology, Microcirculation and as Editorial Advisor for the Biochemical Journal. He has served as Chair of the Translational Sciences Panel of Heart Research UK, Medical Panel of the Henry Smith Charity and on grant panels of the British Heart Foundation, Guy's & St. Thomas' Hospital Charitable Foundation and Royal Society International Networks Panel. He is currently International Lead for the School of Cardiovascular and Metabolic Medicine & Sciences at King's College London. He has coordinated >45 research symposia at international conferences.

Chair: Chang Chen (陈畅)

Institute of Biophysics, Chinese Academy of Sciences, China

Email: changchen@ibp.ac.cn

Short CV

Professor Chang Chen is presently Principal Investigator at Institute of Biophysics, Chinese Academy of Sciences (CAS), Professor of University of CAS, and Vice Director of the NationalLaboratory of Biomacromolecules (2012-2023). She received her BSc from Nankai University in 1990 and her PhD from Peking University in 1996. She then joined the Institute of Biophysics, CAS, and became an independent PI in 2000. She was a visiting scientist at the Institute of Food Research, Norwich, UK with The Royal Society K.C. Wong Research Fellowship from 1998 to 2000 and a visiting scientist at Center for Cancer Research, the Medical Research Council, Cambridge, UK from 2004 to 2005 and at NIH in 2018. Her major research interests are nitric oxide and S-nitros(yl)ation and other thiol modification in redox signaling transduction; redox regulation in aging and the related diseases; mechanism of traditional Chinese medicine.

Chen laboratory demonstrated the important roles of S-nitros(yl)ation in protein quality control, aging and aging-related diseases. They also developed a series of methods for S-nitrosation detection. Their work well illuminates the specificity and the important signalling roles of redox regulation. She proposed the concept of Precision Redox and the "5R" principles as the key for antioxidant pharmacology, i.e., Right species, Right place, Right time, Right level and Right target as guidelines for redox medicine development, defined Redox-stress Response Capacity (RRC) and identified the Redox-stress Signaling Threshold (RST) and discovered the insulin-resistance-like phenomenon in senescent cells, termed Redox-stress Response Resistance (RRR). Then based on RRC/RST/RRR, she advocates to increase RST through early stage exercise to enhance RRC, delay the occurrence of RRR, thereby delay aging as the proactive health strategy. Her lab has demonstrated the mechanisms of the effect of L. barbarum on "strengthening muscle and bone and anti-aging" as recorded in "Ben Cao Gang Mu".

Dr. Chen has been honored National Outstanding Young Scientist and also a receiver of Special Government Allowances of the State Council, China. She is the Chief Scientist of "National Basic Research Program of China, 973 Program" (2006-2010) and the Chief Scientist of "National Key Research and Development Program of China" (2017-2022, 2022-2027). Dr. Chen currently serves the President-elect of SFRR-Asia (Society for Free Radical Research, Asia) and the President of the Society for the Free Radical Biology and Medicine, China. She currently serves as the Associate Editor of Free Radical Biology & Medicine (FRBM)(2019-).

Homepage: http://english.ibp.cas.cn/en_sourcedb_ibp/rck/EN_xsszmA_G/202005/t20200519_341422.html

Plenary Lecture - 2(PL-2)

Warburg Effect Revisited: Role of NRF2 in Pseudohypoxic Stabilization o f HIF-1α

Young-Joon Surh

Seoul National University, Korea

Email: surh@snu.ac.kr

Abstract

The 'Warburg effect' is defined as an increased rate of glucose uptake and glycoloysis even in the presence of oxygen. Hypoxia-inducible factor-1α (HIF-1α) is highly expressed/activated in most tumors including hepatocellular carcinoma (HCC). Another key transcription factor, nuclear factor erythroid 2-related factor 2 (NRF2) is also constitutively overactivated in HCC. In an attempt to determine whether HIF-1α and NRF2 could play complementary roles growth and progression of HCC, we investigated the crosstalk between these two transcription factors and underlying molecular mechanisms in cultured HCC cells and experimentally induced hepatocarcinogenesis as well as clinical settings. While silencing HIF-1α in HepG2 human hepatoma cells did not alter the protein expression of NRF2, NRF2 knockdown markedly reduced the nuclear accumulation of HIF-1α without influencing its mRNA expression. In diethylnitrosamine (DEN)-induced hepatocarcinogenesis, there was elevated NRF2 expression with concomitant upregulation of HIF-1α. However, this was abolished in Nrf2 knockout mice. NRF2 and HIF-1α co-localize and physically interact with each other which was verified by *in situ* proximity ligation and immunoprecipitation assays. In addition, the interaction between NRF2 and HIF-1α as well as their overexpression was found in specimens obtained from HCC patients. In normoxia, HIF-1α undergoes hydroxylation by a specific HIF-prolyl hydroxylase domain protein (PHD), which facilitates ubiquitination and proteasomal degradation of HIF-1α. However, direct interaction with NRF2 hampers the PHD2-mediated hydroxylation and subsequent recruitment of von-Hippel-Linda for ubiquitination of HIF-1α. This results in the stabilization of HIF-1α, even in the presence of oxygen (pseudohypoxia), which may account for the HIF-1α -mediated aerobic glycolysis (Warburg effect).

Key words: HIF-1α, Hepatocellular carcinoma, Hypoxia, NRF2, Pseudohypoxia, Warburg effect

Short CV

Prof. Young-Joon Surh graduated from College of Pharmacy, Seoul National University with Bachelor's and Master's degrees. Prof. Surh earned a PhD degree at the McArdle Laboratory for Cancer Research, University of Wisconsin-Madison. He had postdoctoral training at Massachusetts Institute of Technology (MIT). After spending three and half years as a tenure-track Assistant Professor at Yale University School of Medicine, Prof. Surh relocated to Seoul National University in 1996. Since then, he has been investigating the molecular mechanisms of cancer chemoprevention with anti-inflammatory and antioxidative natural products, with focus on intracellular redox and inflammatory signaling molecules as prime targets. Beside his role as Editor-in-Chief of Journal of Cancer Prevention, Prof. Surh is currently Associate Editor of Toxicology & Applied Pharmacology, Molecular Carcinogenesis, and Free Radical Research, and Editorial Board member of International Journal of Cancer, Cancer Letters, Cancer Prevention Research, Precision Oncology, Molecular & Cellular Biology, Free Radical Biology & Medicine, Antioxidants & Redox Signaling, Genes and Disease, Genes and Nutrition, Molecular Nutrition & Food Research, International Journal of Molecular Sciences, etc. He also co-edited following books: Oxidative Stress, Inflammation and Health (CRC Press), Molecular Targets & Therapeutic Use of Curcumin (Springer-Verlag), and Dietary Modulation of Cell Signaling Pathways (CRC Press). Prof. Surh has published more than 420 papers in peer-reviewed international journals and about 70 invited editorials, reviews and book chapters. The total number of citations of his publications is more than 30,000. The H-Index reported by Thomson Reuter of Web Knowledge is 90. Thomson Reuter selected him as one of the 16 Korean scientists whose publication is most highly cited. Prof. Surh received numerous awards including Elizabeth C. Miller and James A. Miller Distinguished Scholar Award from Rutgers University (2011), McCormic Science Institute Award from American Society for Nutrition (2009), Scientist of the Year Award from the Korea Science Reporters Association (2008), the Korea Science Award given by President of South Korea (2013), etc. He currently serves as President of Society of Free Radical Research-Asia (SFRR-Asia) and Chair of Division of Medical Sciences, Korean Academy of Science and Technology (KAST).

Chair: Malyn Ungsurungsie

S&J Research & Innovation Center, Thailand

Email: malyn_u@snjinter.com

Short CV

Received a Bachelor Degree in Pharmacy from Faculty of Pharmacy, Chulalongkorn University with the Master and Doctorate Degrees in Science (Microbiology), International Program, from Faculty of Science, Mahidol University. Also received a Certificate of Management in Higher Education from Galilee College, Israel and Harvard University Extension School, United States. Had the post-doctorate training at School of Pharmacy, Robert Gordon University, United Kingdom. Followed was a research fellow at Institute of Medical Science, University of Tokyo, and Faculty of Agriculture and Veterinary Medicine, Nihon University, Japan. Had a few-year research experiences at Institute for Biochemical Technology and Microbiology, Vienna University of Technology, Austria.

Started working at Faculty of Pharmacy, Mahidol University and has accomplished to be a full professor. The most recent position is a director of S&J Research & Innovation Center. Additionally, has been appointed as a director and committee member to companies, associations and organizations e.g., S&J (UK) Co., Asian Association of Environmental Mutagen Societies, Silpakorn University, Chiang Mai University.

Received several awards and recognitions e.g., "Invention Award" from National Research Council of Thailand, "Outstanding Industrial Pharmacist" from Thai Industrial Pharmacist Association, "Outstanding Pharmacist" from The Pharmaceutical Association of Thailand Under Royal Patronage, "Outstanding Alumni" from Mahidol University Graduate Study Alumni Association, "Leading Scientists of the World" in the Area of Pharmaceutical Sciences from The Office of the International Biographical Centre, "Cooperation in Narcotic Prevention Award" from Office of the Narcotics Control Board, "Pharmacist Volunteer Certificate of Appreciation" from Her Majesty the Queen Rambhai Barni Medical Mobile Unit.

Plenary Lecture - 3(PL-3)

Gut frailty: its concept and the role of dietary fiber

Yuji Naito

Human Immunology and Nutrition Science, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto 602-8566, Japan

Email: ynaito@koto.kpu-m.ac.jp

Abstract

There is still a considerable gap between average life expectancy and healthy life expectancy in Japan. Recent research has revealed that gut frailty may be an aggravated factor for various diseases, a cause of chronic inflammation, and a precursor to frailty. Among self-reported symptoms, constipation is particularly significant as one of the key symptoms of gut frailty. Studies have demonstrated that individuals with constipation have significantly lower survival rates and are also at a higher risk of developing various diseases such as chronic kidney disease, cardiovascular diseases, and neurodegenerative disorders like Parkinson's disease. Various molecular mechanisms could contribute to gut frailty, and the decrease in mucus secretion is an extremely early-stage pathology. Dysbiosis of gut microbiota has a major impact on many conditions associated with gut frailty. Prebiotics including dietary fibers, probiotics, post-biotics, and fecal microbiota transplantation are under investigation as a treatment option for gut frailty. Although the concept of gut frailty has not yet gained widespread recognition, we hope to propose more practical screening methods, diagnostic approaches, and specific interventions in the future.

Key words: Aging, Gut frailty, Microbiota, Dietary fiber

Short CV

Assistant Professor of Medicine, First Department of Medicine, Kyoto Prefectural University of Medicine, 1998-2000.

Visiting Professor, Department of Molecular and Cellular Physiology, LSU Health Sciences Center, 2001

Associate Professor, Molecular Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine, 2008-2021

Chief, Department of Endoscopy and Ultrasound Medicine, Hospital of Kyoto Prefectural University of Medicine, 2015-2021

Professor, Department of Human Immunology and Nutrition Science, Kyoto Prefectural University of Medicine, 2021-

Chair: Myung Hee Chung

Seoul National University College of Medicine, Korea

Email: mhchung@snu.ac.kr

Short CV

- 1982 ~ 2011: Professor, Pharmacology, Seoul national University College of Medicine
- 2002 ~ 2004: Vice President, Seoul National University
- 2011 ~ 2014: Chair professor, Samsung Medical Center
- 2014 ~ 2018: Vice President for medical Affair, Gachon University
- At Present: Science Adviser, Korea Health Functional Food

Plenary Lecture - 4(PL-4)

Role of CaMKII in heart cell fate regulation

Rui-Ping Xiao (肖瑞平)

College of Future Technology, Peking University, Beijing, China

Email: xiaor@pku.edu.cn

Abstract

Ca^{2+}/calmodulin-dependent kinase II (CaMKII), particularly its predominant isoform in the heart, CaMKII-δ, mediates multiple stress stimuli in the myocardium and is a key regulator of the fate of cardiomyocytes. The excessive activation of CaMKII leads to cardiomyocyte death in conditions such as myocardial infarction, cardiomyopathy, and heart failure. Our findings reveal that receptor-interacting protein 3 (RIP3) activates CaMKII through phosphorylation and oxidation, thereby promoting necroptosis in cardiomyocytes. Inhibition of CaMKII or RIP3 deficiency in mice reduces necroptosis and attenuates heart failure. Furthermore, the CaMKII-δ9 isoform contributes to cardiomyocyte death by impairing DNA repair. Targeting CaMKII oxidation and activity, including using the specific inhibitor hesperadin, presents a promising therapeutic strategy for reducing cardiac damage and related pathologies.

Key words: CaMKII, oxidation/phosphorylation, cardiomyocyte death, necroptosis

Short CV

Dr. Rui-Ping Xiao, a Peking University Chair Professor, is the Dean of the College of Future Technology at Peking University.

Dr. Xiao received her M.D. degree from Tongji Medical University in 1987 and her Ph.D. degree in Physiology from the University of Maryland in 1995. In 2003, she was appointed as a Principal Investigator with tenure of the National Institutes of Health, and in 2010, she returned to China to become the founding Director of the Institute of Molecular Medicine at Peking University.

Dr. Xiao's research has been focused on cardiovascular and metabolic diseases, with an emphasis on a translational approach to bring bench discoveries to clinically relevant situations. Ongoing research directions include signaling pathways involved in Cardiometabolic disease. She served as a Council Member of the International Society of the Heart (ISHR) from 2002 to 2021 and was elected a Fellow of the American Society for Clinical Investigation (ASCI) in 2004. Currently, Dr. Xiao serves as an Associate Editor of the New England Journal of Medicine and an Editorial Board Member of multiple international top journals.

Chair: Jiankang Liu (刘健康)

University of Health and Rehabilitation Sciences, Qingdao, China

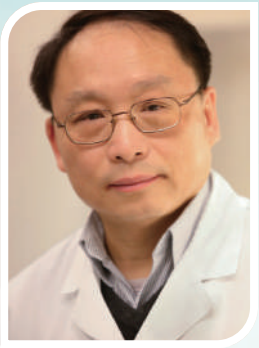
Email: jkliu@uor.edu.cn

Short CV

Dr. Jiankang Liu received his BS from Xi'an Jiaotong Unviersity and PhD of Medical Science from Okayama University School of Medicine, Japan. He completed post-doc training in Dr. Bruce Ames laboratory at University of California, Berkeley and worked as a faculty at University of California at Berkeley, Children Hospital Oakland Research Institute, University of California at Irvine, University of Kentucky College of Medicine, and Shanghai Institute for Nutritional Science, Chinese Academy of Sciences. Currently, he is a Professor of the University of Health and Rehabilitation Sciences at Qingdao and Xi'an Jiaotong University at Xi'an, China. Research interests include molecular and cellular mechanisms of aging, stress, and age-/stress-associated degenerative diseases with a focus on free radical and mitochondrial biology and medicine. Has proposed the "Mitochondrial Free Radical Hypothesis of Stress-induced Aging Acceleration" and "Mitochondrial Nutrients Concept" and published more than 270 peer reviewed papers in SCI journals, 2 books, and 20 book chapters; applied 24 patents; The total citations are 17000 times and H index is 81 (Google Scholar Data of April 10, 2024) and topped consecutively for 10 years (2014-2024) to the list of "Elsevier the Most Cited Chinese Researchers" and the World Top 1.5-2% Scientist (2019-2023).

He worked as Associate Editor for "Nutritional Neuroscience", "Antioxidants" and "Current Topics on Neutraceutical Research", and editorial board member for "Free Radical Biology and Medicine", "Antioxidants and Redox Signaling", "Mitochondrion" "Neurochemical Research", "Basic and Clinical Pharmacology and Toxicology" "Sport Medicine and Health Sciences" etc. As Co-Guest Editor for editing special issues for "Neurochemical Research", "Free Radical Biology and Medicine", "Antioxidants", and "Antioxidants and Redox Signaling".

Plenary Lecture - 5(PL-5)



Energy Matters: Reprogramming of Redox Signaling and Mitochondrial Energy Metabolism in Aged Neurons

Zu-Hang Sheng

National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health, Bethesda, USA

Email: shengz@ninds.nih.gov

Abstract

Mitochondria are the cellular power plants that generate ATP to power various neuronal functions and regeneration. Chronic mitochondrial dysfunction and energy deficits are pathological hallmarks of aging-associated neurodegeneration, while acute mitochondrial damage triggered by brain injury leads to a local energy crisis that contributes to regeneration failure. Therefore, defects in mitochondrial maintenance have emerged as central issues in neurodegeneration and regeneration. I will first overview our recent investigations of reprogramming mitochondrial maintenance and transport and restoring bioenergetic metabolism to power neuronal regeneration and synaptic transmission **(1-13).**

Aging is a key risk factor in the development of neurodegeneration. As postmitotic cells, neurons face exceptional challenges in maintaining energy homeostasis over an organism's lifespan. Recovery of chronically stressed mitochondria is critical to energy maintenance in neuronal aging. Mitochondrial DNA (mtDNA) encodes 13 proteins essential for oxidative phosphorylation and ATP production. Mitochondrial nucleoids (mt-nucleoids) are composed of mtDNA and machineries for mtDNA replication and transcription. Since mitochondria are one of the primary sources of ROS, mt-nucleoids are constantly exposed to an oxidative microenvironment throughout a neuron's life. However, it remains elusive how chronic oxidative stress affects mt-nucleoid integrity and mitochondrial bioenergetics with age. I will introduce our recent work revealing the crosstalk between redox signaling and mitochondrial energy metabolism in aged neurons **(14)**. Using mouse dorsal root ganglion neurons and human iPSC-derived neuronal models, combined with cutting-edge live-cell imaging with mitochondria-targeted ROS and ATP sensors and Seahorse assays, we provide a comprehensive mitochondrial aging profile: neuronal mitochondria from aged mice display increased ROS levels, declined respiratory capacity, and reduced ATP production compared to neurons from young adult mice. Combining phase separation assays, MINFLUX nanoscopy imaging (1-3 nm resolution), AI-based machine learning, and mtDNA transcription/translation analysis, we found that neuronal mt-nucleoids from aged mice are strikingly disorganized both structurally and functionally. Triggering oxidative stress in young neurons recapitulates the aging mt-nucleoid phenotypes. With genetic targeting, we further identified oxidative response elements. Reprogramming oxidation-resistant signaling by replacing the targeted cysteine residue effectively attenuates

the disruption of mt-nucleoid condensates and reverses the declined mitochondrial energy metabolism in neurons from aged mice. Thus, our study provides new mechanistic insights into how chronic oxidative stress in aged neurons adversely affects mitochondrial bioenergetics, offering translational implications for restoring mt-nucleoid phase separation and integrity in normal aging and aging-associated neurodegeneration (Supported by the Intramural Research Program of NINDS, NIH).

Selected Sheng lab publications on neuronal mitochondria and energy metabolism:

1.Cheng XT, Huang N, Sheng ZH, **Neuron**, 2022, 110: 1899.

2.Li S, Sheng ZH, **Nature Reviews Neuroscience** 2022, 23:4.

3.Chamberlain KA*, Huang N* et al., **Neuron** 2021, 109:3456.

4.Huang N et al., **Current Biology** 2021, 31:3098.

5.Li S et al., **Nature Metabolism** 2020, 2:1077.

6.Han Q et al., **Cell Metabolism** 2020, 31:623.

7.Puri R et al., **Nature Communications** 2019, 10:3645.

8.Lin MY*, Cheng XT* et al., **Neuron**, 2017, 94: 595.

9.Zhou B et al., **Journal of Cell Biology**, 2016, 204:103

10.Morsci N et al., **Journal of Neuroscience,** 2016, 36:1373.

11.Xie Y, Zhou B et al., **Neuron** 2015, 87:355.

12.Sun T, Qiao H et al., **Cell Reports**, 2013, 4:413.

13.Kang JS et al., **Cell** 2008, 132:137.

14.Cheng XT*, Gao Y* et al., **unpublished**.

Short CV

Dr. Sheng received his Ph.D. in Biochemistry from the University of Pennsylvania in 1993 and completed his postdoctoral research with William Catterall at the University of Washington in 1996. He joined NINDS as an investigator in 1997 and is now a senior investigator and Chief of the Synaptic Functions Section at NINDS, NIH. Dr. Sheng was elected a Fellow of the AAAS in 2016 and a fellow of the ASCB in 2017. He received the 2021 Dr. Francisco S. Sy Award for Excellence in Mentorship from the US Department of Health and Human Service (HHS) and is the recipient of the 2023 NIH Director's Award for seminal contributions to the understanding of axonal mitochondrial and lysosomal transport and the maintenance of bioenergetics and cellular homeostasis in synaptic transmission and neural regeneration.

Chair: Yan-Zhong Chang (常彦忠)

Hebei Normal University, China

Email: yzchang@hebtu.edu.cn

Short CV

Dr. Yan-Zhong Chang, Professor of College of Life Science in Hebei Normal University. He got his PhD degree in Hong Kong Polytechnic University. From 2008 to 2009, he was a Visiting Professor to study the regulation of brain iron metabolism in Dr. Tracey Rouault's Lab, NICHD. In 2003, he founded the Lab of molecular iron metabolism in Hebei Normal University. He major conducts his research in the mechanisms of iron metabolism, the mechanisms and treatment of iron misregulation and redox imbalance in Parkinson's disease, Alzheimer's disease, stroke, mental and emotional disorders; Preparation and safety evaluation of brain-targeted nanomedicines. As the first author or corresponding author Prof. Chang has published more than 100 papers on peer reviewed international journals such as European Heart Journal, ACS Nano, Redox Biology, and these papers have got more than 5000 citations. As the editor of 'Brain Iron Metabolism and CNS Diseases' was published by the Springer (2019). He is the Advisory Board member of the Journal- Cellular and Molecular Life Sciences. He won the First (2019), Second (2016) and Third (2013) Grade Awards for Natural Science of Hebei Provence.

Special Lecture

Carry forward the cause and forge ahead into the future ——Memory of past 20 years SFRR-Asia biennial meetings

Chang Chen (陈畅)

Institute of Biophysics, Chinese Academy of Sciences, Beijing, China

Email: changchen@ibp.ac.cn

Taking this special opportunity, I would like to review the history and achievement of the Society for Free Radica Research-Asia (SFRR-Asia) and to recall the great memories of the past ten biennial meetings. At the same time, I will share my view of the future development of redox research to attract good ideas. After two decades, we are marching into a new era to explore redox biology and medicine at precision, mechanistic and *in vivo* levels with innovative technology and multiple discipline collaborations. It is the right time to think over the future of redox biology and medicine with regard to the conception, the essential questions, the new strategy and even the research pattern. Concerning the main challenge of redox biology and medicine research, I propose that seven layers (7L) should be explored, aiming "to know redox, to decode redox, and to utilize redox". L1, New technology for precision redox research, particularly an *in vivo*, in situ quantitative approach; L2, Exploring the redox network/family regarding discovery of new redox genes, species, noncoding RNAs, etc. L3, Biochemical mechanism of redox, concerning redox modification of biomacromolecules, redox relay, and redox architecture. L4, Redox regulation in organelle function, quality control and cell fate. L5, Redox physiology in development and reproduction and environmental challenge. L6, Redox stress in the pathogenesis of various diseases. Some uncultivated lands should be addressed, for example, redox signaling in mental health. L7, Precision redox intervention and health management, involving traditional medicine, intelligence materials, lifestyle, nutrition application, drug development, etc. Popularization of science and technology of redox biology and medicine is also one important part for improving public health. To stimulate the 7L research, multidisciplinary global-level collaborations, in both basic and clinical research, need to be implemented.

Chair: Yang Liu (刘扬)

Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

Email: yliu@iccas.ac.cn

Short CV

Yang LIU, B.S. (1982) and M.S (1985) at Tsinghua Univ., Ph.D. (1988) at Inst. of Chem., the CAS; assist. Prof. (1988-1991); Associate Prof. (1991-1992) at Inst. of Chem., the CAS; visiting scientist at Institut für Pharmakol., Veterinämed. Univ. Wien (1992-1997); full Prof. (1997- present) in Inst. of Chem , the CAS & Univ. of CAS.

Awards:

The Natural Science Prize, 1991, in The Chinese Academy of Sciences on the contribution of spin trapping - ESR investigation;

Wang Tian-jiuan Prize, 2000, from the Magnetic Resonance Committee, Chinese Physical Society;

Contribution Award of EPR Development, 2022, from Xu Yuanzhi Award Funds of EPR Development;

Outstanding Contribution Award, 2023, from SFRR-China.

Research Interests

Ø Nanomedicine and drug delivery for oxidative stress-related diseases, such as ischemic stroke, Alzheimer's disease and cancer;

Ø *In vivo* and intracellular ROS/NOS assays with fluorescence probes and microelectrodes;

Ø *In vivo* and intracellular target spin trapping - ESR.

Selected Publications (total publications: 168)

1 Xiaojie Zhang, Xiaoxuan Kang, Libo Du, Lu Zhang, Yan Huang, Jihan Wang, Sihan Wang, Yanzhong Chang*, Yang Liu*, Yuming Zhao*, Tanshinone IIA loaded chitosan nanoparticals decrease toxicity of β-amyloid peptide in a Caenorhabditis elegans model of Alzheimers disease, Free Rad Biol Med, 193: 81–94(2022).

2 Yaru Li, Xiaojie Zhang, Zhifeng Qi*, Xueling Guo, Xiaopeng Liu, Wenjuan Shi, Yang Liu*, LiBo Du*, The enhanced protective effects of salvianic acid A: A functionalized nanoparticles against ischemic stroke through increasing the permeability of the blood-brain barrier, Nano Research , 13: 2791-2802(2020).

3 Xueling Guo, Xiaoxuan Kang, Yueqi Wang, Xiaojie Zhang, Changjian Li, Yang Liu*, Libo Du*. Co-delivery of cisplatin and doxorubicin by covalently conjugating with polyamidoamine dendrimer for enhanced synergistic cancer therapy, Acta Biomaterialia, 84: 367-377(2019)..

4 Shaipeng Huang, Rongchen Han, Qiaofen Zhuang, LiBo Du, Hongying Jia, Yangping Liu, Yang Liu*, New photostable naphthalimide-based fluorescent probe for mitochondrial imaging and tracking. Biosensors and Bioelectronics, 71: 313-321 (2015).

5 Qianfen Zhuang, Hongying Jia, Libo Du, Yanchao Li, Zhao Chen, Saipeng Huang, Yang Liu*. Targeted Surface-functionalized Gold Nanoclusters for Mitochondrial Imaging. Biosensors and Bioelectronics, 55: 76-82 (2014).

6 Lu Han, Libo Du, A Kumar, Hongying Jia, Qiu Tian, Guangjun Nie, Xinghe Liang, Yang Liu*, Inhibitory effects of trolox-encapsulated chitosan nanoparticles on tert-butylhydroperoxide induced RAW264.7 apoptosis, Biomaterials, 33: 8517-8528(2012).

7 Hong-ying Jia, Yang Liu*, Xue-ji Zhang*, Lu Han, Li-bo Du, Qiu Tian, Yuan- chao Xu, Potential Oxidative Stress of Gold Nanoparticles by Induced-NO Releasing in Serum, J Am Chem Soc, 131(1): 40-41 (2009).

8 Zhou Nie, Ke-jian Liu, Chuan-jian Zhong, Lan-fen Wang, Ying Yang; Qiu Tian; Yang Liu*, Enhanced radical- scavenging activity by antioxidant-functionalized gold nanoparticles: A novel inspiration for development of new artificial antioxidant, Free Rad Biol Med, 43: 1243–1254(2007)

Symposium-1(S1)

Redox signaling in organelles/cell fate/development/reproduction

Chair: Taotao Wei (卫涛涛)

Institute of Biophysics, Chinese Academy of Sciences, China

Email: weitt@ibp.ac.cn

Short CV

1989 - 1993 BSc, Huazhong University of Science and Technology

1993 - 1996 MSc, Hubei Institute of Chemistry

1996 - 1999 PhD, Institute of Biophysics, Chinese Academy of Sciences

1999 - 2001 Assistant Professor, Institute of Biophysics, Chinese Academy of Sciences

2001 - 2008 Associate Professor, Institute of Biophysics, Chinese Academy of Sciences

2008 - Professor, Institute of Biophysics, Chinese Academy of Sciences

Mitochondrion is the center for energy metabolism machinery, and the major checkpoint of apoptotic regulation. The homeostasis of mitochondrial network plays essential role in many cellular processes; its dysregulation has been linked to many diseases. We aim to use combined approaches to investigate the mechanism and regulation of the mitochondrial network, and their implication in various human diseases.

Selected papers:

[1] CRISPR screening uncovers nucleolar RPL22 as a heterochromatin destabilizer and senescence driver. Nucleic Acids Research, (2024), doi.org/10.1093/nar/gkae740.

[2] Structural and biochemical insights into the mechanism of the Gabija bacterial immunity system. Nature Communications, 15(2024), 836.

[3] Airway relaxation mechanisms and structural basis of osthole to improve lung function in asthma. Science Signaling, 13(2020), eaax0273.

[4] KAP1-associated transcriptional inhibitory complex regulates C2C12 myoblasts differentiation and mitochondrial biogenesis via miR-133a repression. Cell Death and Disease 11(2020), 732.

[5] Transforming growth factor (TGF)-β1-induced miR-133a inhibits myofibroblast differentiation and pulmonary fibrosis. Cell Death and Disease 10(2019), 670.

[6] Detection of tBid oligomerization and membrane permeabilization by graphene-based dingle-molecule surface-induced fluorescence attenuation. Nano Letters 19(2019), 6937-6944.

[7] YWHA/14-3-3 proteins recognize phosphorylated TFEB by a noncanonical mode for controlling TFEB cytoplasmic localization. Autophagy 15(2019), 1017-1030.

[8] SIRT5 deacylates metabolism-related proteins and attenuates hepatic steatosis in ob/ob mice. EBioMedicine 36(2018), 347-357.

H_2O_2 promotes stomatal development and opening through regulating SnRK1

Mingyi Bai (白明义)

Shandong University, China

Email: baimingyi@sdu.edu.cn

Abstract

Stomata are plant-specific epidermal structures that function as the main conduit for water vapor and carbon dioxide exchange between plant and atmosphere. The formation and movement of stomata is regulated by multiple developmental and environmental signals. Here, we showed that spatially patterned hydrogen peroxide (H_2O_2) plays essential roles in stomatal development and light-induced stomatal opening through regulating the nucleocytoplasmic shuttling of KIN10, the catalytic α-subunit of energy sensor kinase SnRK1. H_2O_2 is remarkably enriched in meristemoids and guard cells, which is established by spatial expression patterns of H_2O_2-scavenging enzyme CAT2 and APX1. H_2O_2 interferes the interaction between KIN10 and the regulator subunit KINβ2, and then promotes the nuclear localization of KIN10. In stomatal lineage cells, KIN10 phosphorylates and stabilizes SPCH, a master regulator of stomatal formation, thereby promoting stomatal development. In guard cells, KIN10 phosphorylates a bZIP transcription factor KIP1, which specifically expresses in guard cells. KIN10-mediated phosphorylation of KIP1 enhances its transcriptional activity on BAM1 and KAT1, thereby promoting stomatal opening upon light exposure. The spatial distribution pattern of H_2O_2 in meristemoids and guard cells was found not only in Arabidopsis leaves but also in wheat leaves. H_2O_2 also plays an essential role for light-induced stomatal opening in wheat leaves. Overall, these evidences uncover the conservative roles of H_2O_2 in promoting stomatal development and stomatal opening in monocotyledon and dicotyledon plants.

Key words: H_2O_2, SnRK1, Brassinosteroid, Stomatal development, Stomatal opening

Short CV

Prof. Mingyi Bai earned his Ph.D. from the Institute of Botany, CAS, in 2007 and completed postdoctoral training at the Carnegie Institution for Science in Zhi-Yong Wang's lab. In 2014, he was appointed as a Principal Investigator at Shandong University. His research focuses on how the phytohormone brassinosteroid regulates plant growth and stress responses. Notable achievements include elucidating the role of brassinosteroids (BR) in the nitrate signaling pathway, detailing BR-mediated guard cell starch metabolism in stomatal movement, and uncovering the crucial role of hydrogen peroxide (H_2O_2) in BR signaling. His work has been published in top journals such as Nature Plants, Nature Communications, and Plant Cell, and has been featured in Preview. Prof. Bai has received several awards, including the National Science Fund for Distinguished Young Scholars, the Shandong Province Science Fund for Distinguished Young Scholars, and the Young Thousand Talents program. He also serves as an editor for JIPB, New Crops, and Frontiers in Plant Science.

Artemisinin attenuates astrocyte overactivation by inhibiting IRE1 phosphorylation and the downstream NF-κB pathway in Alzheimer's disease

Wenhua Zheng (郑文华)

Department of Pharmacology, Faculty of Health Sciences, University of Macau, China

Email: wenhuazheng@um.edu.mo

Abstract

Alzheimer's disease (AD) is characterized by the accumulation of amyloid-beta (Aβ) and is associated with neuroinflammation, endoplasmic reticulum (ER) stress and cognitive decline. Abnormal accumulation of β amyloid peptide (Aβ) induces ER stress, activating astrocytes through the nuclear factor kappa-B (NF-κB) pathway and ultimately causing neuroinflammation and neuronal injury. Astrocyte dysfunction can disrupt the normal neuronal environment, which is essential for maintaining cognitive function. Therefore, targeting the modulation of the ER stress-inflammatory cycle and normalizing astrocyte function could be a potential strategy for AD. Recent studies indicate that artemisinin has significant neuroprotective effects. However, the mechanism by which artemisinin regulates astrocyte activation to improve AD process requires further exploration. We investigated the impact of Aβ1-42 on astrocyte activation and explored the potential therapeutic effects of artemisinin (ART) *in vitro* and in a 3×Tg-AD mouse model.

Exposure of A172 cells to Aβ1-42 induced astrocyte activation, endoplasmic reticulum (ER) stress, and inflammatory responses. ART treatment attenuated these effects, specifically inhibiting IRE1 phosphorylation and downstream NF-κB signaling. ART also restored the neurotrophic function of astrocytes, protecting primary neurons from Aβ1-42 toxicity. The IRE1 kinase inhibitor KIRA6 reversed the toxic effects of Aβ1-42 on astrocytes, emphasizing the role of IRE1 in neuroinflammation.

In further studies, we demonstrated that ART's neuroprotective effects were mediated through the IRE1-ER stress pathway. It relied on IRE1 kinase activity to prevent Aβ1-42-induced astrocyte overactivation, confirmed by IRE1 wild-type and mutant plasmid experiments. Additionally, ART restored the phosphatase activity of PP2A, inhibiting IRE1 phosphorylation.

To validate these findings *in vivo*, 3×Tg-AD mice were treated with ART. ART reduced IRE1-mediated downstream inflammatory signals, alleviated astrocyte overactivation, and rescued neuronal apoptosis. It also ameliorated cognitive deficits in these mice. Pharmacological interventions in the mouse model further supported ART's therapeutic potential by demonstrating improvements in cognitive function and reduced neuroinflammation. Importantly, AAV-mediated IRE1 overexpression in astrocytes abrogated the beneficial effects of ART, highlighting the critical role of IRE1 in mediating ART's neuroprotective effects.

In conclusion, our study demonstrates that artemisinin exerts neuroprotective effects by modulating the IRE1-ER stress pathway in astrocytes, reducing neuroinflammation, and ameliorating cognitive deficits in an AD mouse model. These findings provide insights into the potential therapeutic value of artemisinin in Alzheimer's disease.

Short CV

Dr. WenHua Zheng, Professor, Principle Investigator in the Faculty of Health Science, University of Macau, leading a group of scientists working on aging and neuronal degenerative disorders, including Alzheimer's disease and degenerative retinal diseases; New functions and downstream targets of FoxO; Protective effect of Artemisinin and new drug developments. He is a Section Editor for Encyclopedia of Gerontology and Population Aging and a Lead Guest Editor and Editor for several journals. He is a grant Reviewer for NSFC, Poland, and CIHR in Canada. He is the Honorable Professor at the University of Queensland (QS45) and an Adjunct Professor/Visiting Prof at RMIT University in Australia and other universities at home and abroad. Dr Zheng has published >150 papers, which have been cited over 5000 times (Google >9000).

Redox Signal Regulation by Supersulfides

Takaaki Akaike

Department of Environmental Medicine and Molecular Toxicology, Tohoku University Graduate School of Medicine, Japan

Email: takaike@med.tohoku.ac.jp

Abstract

The major focus of redox biology has been on molecular oxygen, the most abundant element of the planet. The oxygen molecule accepts electrons from the respiratory chain in the mitochondria and is responsible for energy production in aerobic organisms. In addition, oxygen-derived reactive oxygen species that include hydrogen peroxide and oxygen- and nitrogen-centered free radicals, such as superoxide, hydroxyl radical and nitric oxide, undergo a complicated way of electron transfer reactions through their interaction with other biological substances, leading to alteration of their physiological functions, and cause diverse biological and pathophysiological consequences like oxidative stress. Discovery of supersulfides helped us to realize that the oxygen molecule itself accounts only partly for the redox reaction in many organisms, even under aerobic or hypoxic conditions, however, while it is much less biologically relevant in anaerobic and anoxic environments. My talk will deal with a brand-new venue of redox biology, which is governed by the redox-active supermolecules that are mostly consisted of supersulfides, i.e., sulfur-catenated molecular species. They are now found abundantly in all organisms but remain largely unexplored in view of the redox biology and life science research. In fact, accumulating evidence show that supersulfides are electron rich and thereby readily ionized or radicalized, so that they can actively participate in the energy metabolism, redox dependent signaling, and oxidative stress responses in the cellular and *in vivo* context. Moreover, the pharmacological intervention and medicinal manipulation of supersulfides has been shown to be beneficial in prevention as well as regulation of disease pathogenesis. The supersulfide biology now open up a new era of disease control that includes its potential application to clinical diagnosis, prevention, and therapeutics for various diseases.

Key words: Persulfides, polysulfides, supersulfides, redox signaling

Short CV

1992 Assistant Professor, Department of Microbiology, Kumamoto University School of Medicine;1993 Visiting Professor, Department of Microbiology and Immunology, Center for Neurovirology, Thomas Jefferson University; 1994 Associate Professor, Department of Microbiology, Kumamoto University School of Medicine; 2001 Visiting Professor at Center for Free Radical Research, University of Alabama at Birmingham; 2003 Program Officer at the Ministry of Education, Science, Sports and Culture (MEXT) of Japan; 2013 Full Professor, Department of Microbiology, Graduate School of Medical Sciences, Kumamoto University; 2013 Vice Dean & Director of Center for Medical Education and Research at Kumamoto University Medical School; 2019 Vice Dean, Tohoku University Graduate School of Medicine and Tohoku University Medical School; 2013-present Full Professor and Chair, Department of Environmental Medicine and Molecular Toxicology, Tohoku University Graduate School of Medicine

Carbon monoxide sensitizes cancer cell to erastin-induced ferroptosis via ROS-PERK-ATF4

Hun Taeg Chung

College of Korean Medicine, Daegu Haany University, Gyeongsan 38610, Korea

Email: chunght@dhu.ac.kr

Abstract

Ferroptosis is an emerging form of regulated cell death, distinct from traditional apoptosis, characterized by iron-dependent lipid peroxidation. Carbon monoxide (CO), an endogenously gaseous molecule that is generated via the catabolism of heme by heme oxygenase 1 (HO-1), induces mitochondrial ROS-mediated activation of PERK, an arm of unfolded protein response (UPR). Because CO produces ROS and activates PERK which is known to be activated during ferroptosis, we tested whether CO could affect the ferroptosis inducer -mediated ferroptosis. We found that CO increases ferroptosis susceptibility of cancer cells even though its mechanism is not definitely identified. We observed that PERK was highly activated by CO in dose-dependent manner and in turn, sensitized cancer cells to erastin-induced ferroptotic cell death. Moreover, CO-mediated activation of PERK-ATF4 pathway leads to an increase in ferroptosis marker PTGS2 expression and lipid ROS. Additionally, ATF4-driven upregulation of CHAC1 and REDD1 resulted in the depletion of glutathione (GSH) and suppression of mTORC1 and GPX4, respectively, further promoting ferroptosis. The deficiency of PERK abrogated CO-induced ferroptosis sensitivity. These results reveal that the CO-PERK-ATF4 axis plays a crucial role in sensitizing cancer cells to erastin-induced ferroptosis, offering potential therapeutic avenues for enhancing ferroptosis-based cancer treatments.

Short CV

· 2024~ present: Professor, Daegu Haany University, Republic of Korea

· 2009~2023: Professor, University of Ulsan, Republic of Korea

Oxidative phosphorylation, H_2O_2 production, mitochondrial membrane potential, coenzyme Q redox state, and calcium uptake: from tissue normoxia to deep hypoxia

Erich Gnaiger

Beijing Huawei Zhongyi Technology Co. Ltd

Abstract

Mitochondrial respiration extends beyond ATP generation, with the organelle participating in many cellular and physiological processes. Parallel changes in components of the mitochondrial electron transfer system with respiration render it an appropriate hub for coordinating cellular adaption to changes in oxygen levels. How changes in respiration under functional hypoxia (i.e., when intracellular O_2 levels limit mitochondrial respiration) are relayed by the electron transfer system to impact mitochondrial adaption and remodeling after hypoxic exposure remains poorly defined. This is largely due to challenges integrating findings under controlled and defined O_2 levels in studies connecting functions of isolated mitochondria to humans during physical exercise. Here we present experiments under conditions of hypoxia in isolated mitochondria, myotubes and exercising humans. Performing steady-state respirometry with isolated mitochondria we found that oxygen limitation of respiration reduced electron flow and oxidative phosphorylation, lowered the mitochondrial membrane potential difference, and decreased mitochondrial calcium influx. Similarly, in myotubes under functional hypoxia mitochondrial calcium uptake decreased in response to sarcoplasmic reticulum calcium release for contraction. In both myotubes and human skeletal muscle this blunted mitochondrial adaptive responses and remodeling upon contractions. Our results suggest that by regulating calcium uptake the mitochondrial electron transfer system is a hub for coordinating cellular adaption under functional hypoxia.

Symposium-2(S2)

Redox and aging ① “Targeting Redox and Mitochondria to delay aging and prevent age-related diseases”Forum

Chair: Ke Liu (刘科)
Sichuan University, China
Email: kliu@scu.edu.cn

Short CV

Education

Ph.D. in Chemistry, Institute of Chemistry CAS, Beijing, China (2001)
M.S. in Biochemistry, Sichuan University, Chengdu, China (1998)
B.S. in Biochemistry, Sichuan University, Chengdu, China (1995)

Research Interests

My research focuses on understanding the molecular and cellular mechanisms of aging and age-related diseases, particularly exploring the connection between redox signaling and chronic diseases. I also work on developing methods to counteract aging using biochemical interventions.

Professional Experience

Professor: College of Life Science, Sichuan University (2005–Present)
Post-doctoral Scholar: The Jean Mayer USDA Human Nutrition Research Center, Tufts University (2010–2012)
Post-doctoral Assistant: Department of Biochemistry, University of Kentucky (2001–2005)

Selected Publications

1. Liu K, Zhang X, Lester RL, Dickson RC. The sphingoid long chain base phytosphingosine activates AGC-type protein kinases in Saccharomyces cerevisiae including Ypk1, Ypk2, and Sch9. J Biol Chem. 2005 Jun 17;280(24):22679-87.

2. Liu J, Huang X, Withers BR, Blalock E, Liu K, Dickson RC. Reducing sphingolipid synthesis orchestrates global changes to extend yeast lifespan. Aging Cell. 2013 Oct;12(5):833-41.

3. Liu K, Lyu L, Chin D, Gao J, Sun X, Shang F, Caceres A, Chang ML, Rowan S, Peng J, Mathias R, Kasahara H, Jiang S, Taylor A. Altered ubiquitin causes perturbed calcium homeostasis, hyperactivation of calpain, dysregulated differentiation, and cataract. Proc Natl Acad Sci U S A. 2015 Jan 27;112(4):1071-6.

4. Liu B, Wang W, Shah A, Yu M, Liu Y, He L, Dang J, Yang L, Yan M, Ying Y, Tang Z, Liu K. Sodium iodate induces ferroptosis in human retinal pigment epithelium ARPE-19 cells. Cell Death Dis. 2021 Mar 3;12(3):230.

Homepage

Google Scholar Profile：https://scholar.google.com/citations?user=bvAp5agAAAAJ&hl=en

Vitamin A treatment rescues retinal cell-specific deficiencies caused by Leber's hereditary optic neuropathy-linked mtDNA mutation

Minxin Guan (管敏鑫)

Zhe Jiang University, China

Email: gminxin88@zju.edu.cn

Abstract

Leber hereditary optic neuropathy (LHON) is a paradigm for mitochondrial retinopathy due to mitochondrial DNA (mtDNA) mutations. However, the mechanism underlying retinal cell-specific effects of LHON-linked mtDNA mutations remains poorly understood and there has been no effective treatment or cure for this disorder. Using a mice model bearing a LHON-linked ND6P25L mutation, we demonstrated that the mutation caused retinal cell-specific deficiencies, especially in retinal ganglion cells (RGC), rods and Müller cells. Single-cell RNA sequencing revealed cell-specific dysregulation of oxidative phosphorylation and visual signaling pathways in the mutant retina. Strikingly, ND6 mutation-induced dysfunctions yielded abnormal vitamin A (VA) metabolism essential for visual function. VA supplementation remarkably alleviated retinal deficiencies, including reduced fundus lesion and retinal thickness, and increasing numbers of RGCs, photoreceptors and Müller cell neurites. The restoration of visual functions with VA treatment were further evidenced by correcting dysregulations of phototransduction cascade and neurotransmitter transmission and restoring electrophysiological properties. Interestingly, VA supplementation markedly rescued the abnormal mitochondrial morphologies and functions in the mutant retina. These findings provide new insight into retina-specific pathophysiology of mitochondrial retinopathy arising from vitamin A deficiency and mitochondrial dysfunction induced by mtDNA mutation and step toward for therapeutic intervention for LHON and other mitochondrial retinopathies.

Short CV

Dr. Min-Xin Guan graduated with BS in biology from Hangzhou University (previous and current Zhejiang University) in 1983. He did his postgraduate study at the Australian National University (Ph.D. 1993; Advisor: Professor G. Desmond Clark-Walker). Dr. Guan conducted postdoctoral research in the laboratory of Professor Giuseppe Attardi at the California Institute of Technology (1993-1999). In 1999, he started his independent research as an assistant professor at Cincinnati Children's Hospital Medical Center and the University of Cincinnati, eventually becoming a full professor in Division of Human Genetics, Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine in 2011. Since 2011, he has been joining the faculty at Zhejiang University as the founding Director of Institute of Genetics, Dean of College of Life Sciences (2011-2013), Associate Dean of Faculty of Medicine and Pharmaceutical Sciences (2015-2022). Dr. Guan's research interests focus on human mitochondrial genetics and biomedicine. Guan's pioneering work with mitochondrial diseases included the discoveries of the mitochondrial cause of maternally inherited nonsyndromic and aminoglycoside induced hearing loss. Dr. Guan's recent pioneering work were the finding how the interactions between mtDNA mutations and nuclear modifiers manifested the deafness and Leber's hereditary optic neuropathy. Currently, Dr. Guan's lab is focusing on investigating the mechanisms underlying the aberrant mitochondrial tRNA metabolisms including the synthesis, processing, maturation, CCA addition, posttranscriptional nucleotide modification and aminoacylation of tRNA, and their impact on human diseases including deafness, optic neuropathy and hypertension. Dr. Guan has published 184 manuscripts on mitochondrial diseases in the high impact journals. Dr. Guan served as the 4th president of Asian Society of Mitochondrial Research and Medicine (2011-2014).

Cardiolipin Remodeling byALCAT1 Controls the Mitochondrial Free Radical Clock

Yuguang Shi (史裕光)

Barshop Aging Institute, UT-Health, San Antonio, USA

Email: shiy4@uthscsa.edu

Abstract

Aging is the primary cause for all age-related chronic disorders. Although the underlying causes remain poorly understood, aging increases oxidative stress that leads to the production of high level of reactive oxygen species (ROS). ROS cause cumulative damages to mitochondrial membrane proteins, phospholipids, and mitochondrial DNA, which is coined as the "the Mitochondrial Free Radical Aging Clock (MFRAC)" that links mitochondrial dysfunction associated with aging to the development of age-related chronic diseases, such as type 2 diabetes, heart failure, stroke, and neurodegenerative diseases. Despite of intensive efforts in recent years, what controls the MFRAC remains the last frontier in biomedical research. Our pioneering work in the field has identified ALCAT1 as the key regulator of the MFRAC. Our groundbreaking work show that induction of ALCAT1 by ROS accelerates the MFRAC by catalyzing pathological remodeling of cardiolipin with very long polyunsaturated fatty acids (PUFAs). Cardiolipin is the mitochondrial signature phospholipid that is required for every aspect of mitochondrial biology, from membrane structure, oxidative phosphorylation, mtDNA biogenesis, to mitochondrial fusion, fission, and mitophagy. Enrichment of cardiolipin with PUFAs renders cardiolipin highly sensitive to oxidative damages by ROS, leading to mitochondrial dysfunction in metabolic tissues with high energy demand from oxidative phosphorylation. Using mice with targeted deletion of ALCAT1 and Dafaglitapin, an extremely potent and highly selective ALCAT1 inhibitor, we demonstrated that age-related disorders can be treated as one disease, a paradigm-shifting concept for aging research.

Short CV

Dr. Roger (Yuguang) Shi is currently a Joe R. & Teresa Lozano Long Distinguished Chair Professor in Metabolic Biology at Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center at San Antonio (UTHSCSA). His led a unique career path that encompasses a pharmaceutical research experience at Eli Lilly and Company and academic positions at various academic institutions. His laboratory pioneered the cloning of the PERK kinase, a milestone work in ER-stress and translational control, and several first in class enzymes that catalyze the remodeling of phospholipids, including ALCAT1 and LPGAT1. His longstanding research interests in translation medicine has led to the identification of ALCAT1 as the key enzyme that controls mitochondrial etiology of aging and age-related metabolic diseases, including type 2 diabetes, obesity, diabetic complications, cardiovascular diseases, and neurodegenerative diseases. He is a co-founder of Perenna Pharmaceuticals Inc which successfully developed Dafaglitapin, an extremely potent and highly selective ALCAT1 inhibitor. In preclinical studies, Dafaglitapin demonstrated high efficacy in treating all age-related diseases. This pioneering work has validated a paradigm-shifting concept that all age-related metabolic diseases can be treated as ONE disease. His previous research work at Penn State University uncovered a novel signaling pathway by which GLP-1 regulates glucose-sensing by pancreatic beta cells. During his tenure at Lilly, he helped the company to build a robust drug pipeline for type 2 diabetes and obesity, including the successful launch of Byetta (Exenatide), the first-in-class treatment for type 2 diabetes.

A new mode of mitochondria-lysosome contacts under hypoxia

Zhiyin Song (宋质银)

School of Basic medicine, Tongji Medical College, Huazhong University of Science and Technology, China

Email: songzy@hust.edu.cn

Abstract

Mitochondria physically and functionally interact with lysosomes to regulate cellular metabolism. However, the mode and biological functions of mitochondria-lysosome communication remain largely unknown. Here, we show that hypoxia remodels normal tubular mitochondria into megamitochondria by inducing broad inter-mitochondria contacts and subsequent fusion. Importantly, under hypoxia, mitochondria-lysosome contacts are promoted, and certain lysosomes are engulfed by megamitochondria, in a process we term "megamitochondria engulfing lysosome (MMEL)". Intriguingly, MMEL mediates a new mode of mitochondrial degradation, which we termed "mitochondrial self-digestion (MSD)". Moreover, MSD increases mitochondrial ROS production. Our results reveal a novel mode of crosstalk between mitochondria and lysosomes and uncover a new pathway of mitochondrial degradation.

Key words: mitochondria, lysosome, mitochondria-lysosome contacts, mitochondrial self-digestion

Short CV

Zhiyin Song received Ph.D. degree from University of Science and Technology of China in 2005, he then did her post-doctoral training in California Institute of Technology (Caltech) between 2005-2010. Zhiyin Song became a professor in College of Life Sciences at Wuhan University in between 2010-2023, and in Huazhong University of Science and Technology in 2024. Zhiyin Song's research interest is in the area of mitochondrial dynamics and quality control.

Mitochondrial electron transfer chain (ETC) in aging and longevity

Yidong Bai

University of Texas Health San Antonio, USA

Email: baiy@uthscsa.edu

Abstract

Naked Mole-Rats (NMR, Heterocephalus glaber) are the longest-lived rodent species, with a maximum life span of more than 30 years. These long-lived mammals also exhibit delayed aging phenotypes and resistance to age-related pathologies including neurodegeneration. Multiple regulatory pathways have been proposed for the anti-aging mechanisms in NMR including enhanced mitochondrial function and suppressed oxidative stress. In this study, we investigated the assembly of the electron transfer chain (ETC) which constitute the structural base for the regulation of both oxidative phosphorylation and production of reactive oxygen species (ROS), in brains from young and old NMR and C57BL/6 mice. While ETC assembly declined with aging in C57BL/6 mice, we found that NMR displays a robust respiratory chain assembly at older ages in both males and females. Among them, individual complex IV and supercomplexes containing Complex I and III, and complex III and IV showed the most pronounced differences between two species. Our results indicate that a preserved robust assembly of ETC during aging contributes to enhanced mitochondrial oxidative phosphorylation and suppressed oxidative stress which may contribute to the longevity and resistance to age-related pathologies in NMRs.

Key words: electron transfer chain (ETC), aging, assembly, supercomplex

Short CV

Yidong Bai graduated from Fudan University with a bachelor's degree in microbiology and enrolled in graduate program in Shanghai Institute of Cell Biology, CAS before moving to Columbia University for the PhD program. After a postdoctoral fellowship at Caltech, he moved to the University of Texas Health as a faculty member where he is a professor in the department of Cell Systems and Anatomy.

Dysregulation of hydrogen peroxide-mediated responses to contractile activity in skeletal muscle loss associated with aging

Malcolm J Jackson

Department of Musculoskeletal and Ageing Science, University of Liverpool, Liverpool, L7 8TX, U.K

Email: mjj@liverpool.ac.uk

Abstract

Attenuated responses to redox stress are a common feature of aged organisms and these appear to present in skeletal muscle as a reduced ability to respond to contractile activity. Contracting skeletal muscle generates superoxide from membrane-localised NADPH oxidases and this is rapidly converted to hydrogen peroxide (H_2O_2) which acts to stimulate specific adaptive responses. The nature of these responses is extensive and includes increased generation of stress proteins and upregulation of mitochondrial biogenesis. The concentration of H_2O_2 generated within muscle fibres appears insufficient to directly oxidise redox-sensitive proteins in key response pathways and recent data indicate that effector proteins, such as peroxiredoxins, may play a key role in mediating adaptations. These pathways are disrupted in ageing models and conditions of disuse atrophy but appear amenable to manipulation through pharmacological approaches. Understanding the specific mechanisms involved therefore provides a potential route for interventions to maintain muscle mass and function in multiple degenerative skeletal muscle conditions.

Supported by UKRI Medical Research Council, US National Institute on Aging, Versus Arthritis and the UK Space Agency.

Key words: Skeletal muscle, Ageing, Redox Biology, Reactive Oxygen Species

Short CV

Professor Malcolm Jackson is a research professor at the University of Liverpool. He has an extensive research interest in ageing and frailty and has published over 200 original scientific papers. He has previously been Head of the Institute of Ageing and Chronic Disease (2010-15) and Director of the MRC-Arthritis Research UK Centre for Integrated Research into Musculoskeletal Ageing (CIMA), a UK Centre of Excellence. He has also been Treasurer and President of SFRR-Europe and President of SFRR-International. He has editorial roles with Free Radical Biology and Medicine, Redox Biology and Physiological Reviews.

Symposium-3(S3)

Redox and obesity, vascular function and metabolism

Chair: Zhongbing Lu (陆忠兵)

University of Chinese Academy of Science, China

Email: luzhongbing@ucas.ac.cn

Short CV

Education:

2003–2006	Institute of Biophysics, CAS	Ph.D., Biophysics
2000-2003	Sichuan University	M.S., Biochemistry
1996-2000	Sichuan University	B.S., Biochemistry

Research Position:

2012-	University of Chinese Academy of Sciences, Professor	
2009-2012	University of Minnesota	Research Associate
2006-2009	University of Minnesota	Postdoctoral Associate

Our research is focused on the role of oxidative stress in the pathogenesis of cardiovascular or metabolic diseases.

Selected Publications:

1.Redox Biology. 2024, 70:103080

2.Acta Pharmaceutica Sinica B. 2023, 13(8): 3352-3364

3.Cellular & Molecular Immunology. 2022, 19(12):1333-1346

4.Redox Biology. 2022, 49:102224

Homepage: http://people.ucas.ac.cn/~0019068?language=en

ER oxi-lipidosis drives MASH pathogenesis

Xiao-Wei Chen (陈晓伟)
Peking University, China
Email: xiaowei_chen@pku.edu.cn

Short CV

Dr. Xiao-Wei Chen is the Boya Distinguished Professor of Molecular Medicine at the Peking University. He originally obtained his BS and BA from the Peking University, and completed his Ph.D. training with Dr. Alan Saltiel on metabolic biology at the University of Michigan. He then pursued postdoctoral study on genetics and cardiovascular biology in the laboratory of Dr. David Ginsburg, before being recruited back to the Peking University in 2014. Dr. Chen's work focuses on the genetics and cell biology of lipoprotein biology and lipid homeostasis, particularly by elucidating a receptor-mediated export program for the lipoproteins and identifying the long-sought biogenic lipid scramblase. He has also discovered a messenger role of manganese in lipid control, and conceptualized manganese therapy for intensive plasma lipid lowering to reverse exiting atherosclerotic plaques in disease models. He has published ~70 scientific papers and authored two book chapters. He is the recipient of the Young Investigator Award from the Chinese American Diabetes Association and Special Recognition Award from the Society of Heart and Vascular Metabolism, as well as the Earl Stadtman Scholar finalist from the National Institute of Health, USA and the Distinguished Young Scholar Award from the National Natural Science Foundation, China. He serves as an associate editor at the Biochemical Journal and on the editorial boards of Life Metabolism, Journal of Lipid Research, and Cell Metabolism.

Gut microbial enzymes: new targets for intervention in metabolic diseases

Changtao Jiang (姜长涛)

Department of Immunology, School of Basic Medical Sciences, Peking University, Beijing, 100191, China

Email: jiangchangtao@bjmu.edu.cn

Abstract

Microbial enzymes are key functional molecules of gut microbiota. We have focused on gut microbial enzymes and metabolic diseases. We firstly proposed a new concept of "microbial-host isozymes". By establishing a high-throughput isozyme screening system, we found that microbial-host isozymes are widely present in human. Microbial DPP4, a highly active microbial-host isozyme, can degraded active GLP-1 and cause imbalances in glucose homeostasis, leading to inter-individual differences in host DPP4 inhibitor sitagliptin clinical efficacy. Further, we developed the first microbial DPP4 inhibitor and achieved encouraging results in clinical trials. Microbial bile acid converting enzymes serve as one of the key mediators of interactions between gut microbiota and human. Recently, by constructing a new microbial bile acid mining system based on click chemistry enrichment strategy and untargeted metabolomics, we discovered a new type of microbial bile acids modification—3-acylation modification. Taking advantage of our intestinal strains resource libraries, we identified Bacteroides uniformis as the producer of 3-susCA. Then, we analyzed and verified the key enzyme, BAS-suc, responsible for synthesis of 3-sucCA in B. uniformis based on activity-based protein profiling. Finally, we elucidated the mechanism that the B. uniformis-mediated microbial interactions can improve NASH outcomes through BAS-suc. All in all, we propose a new theory of "cross-kingdom regulation of host homeostasis by gut microbial enzymes".

Key words: metabolic disease; gut microbial enzymes; microbial-host isozymes; bile acid

Short CV

Changtao Jiang, Ph.D., is a tenured full professor at Peking University, serving as the chair of Department of Immunology and the deputy dean of the School of Basic Medical Sciences. He is the recipient of The National Science Fund for Distinguished Young Scholars and XPLORER PRIZE. His work aims at gut microbiota, their microbial enzymes and their impact on metabolic diseases. In short, he pioneers a new theory of "cross-kingdom regulation of host homeostasis by gut microbial enzymes". The research results include the following: proposing a new concept of "microbial-host isozymes"; revealing a novel bile acid modification type and elucidating the role of microbial bile acid converting enzymes in non-alcoholic steatohepatitis (NASH); uncovering a nicotine-degrading gut bacterium and its protective role in NASH. He has published more than 30 SCI papers in Cell (2024), Science (2023), Nature (2022), and other journals, among which, 6 papers are highly cited papers, one paper is picked up by F1000Research and 11 papers are highlighted and by internationally recognized scholars in the field. He is also invited to serve on the editorial board of Cell Metabolism. He has obtained Top 10 Chinese life scientific advances, First prize of Beijing Science and Technology (the first finisher), China Youth Science and Technology Award and C.C. Tan Life Science Awards. He is supported by Major Program of National Natural Science Foundation of China, and State Key Program of National Natural Science of China.

Obstructive sleep apnea syndrome and hepatic lipid metabolism disorders

Junli Liu (刘军力)

Shanghai Jiao Tong University, China

Email: liujunli@sjtu.edu.cn

Abstract

Obstructive sleep apnea syndrome (OSAS), characterized by chronic intermittent hypoxia (CIH), is an independent risk factor for aggravating non-alcoholic steatohepatitis (NASH). The prevailing mouse model employed in CIH research is inadequate for the comprehensive exploration of the impact of CIH on NASH development due to reduced food intake observed in CIH-exposed mice, which deviates from human responses. To address this issue, we conducted a pair-feeding investigation with CIH-exposed and normoxia-exposed mice. We revealed that CIH exposure aggravated DNA damage, leading to hepatic fibrosis and inflammation. Our analysis of genome-wide association study (GWAS) data also disclosed the association between Eepd1, a DNA repair enzyme, and OSAS. Furthermore, we revealed that CIH triggered selective autophagy, leading to the autophagic degradation of Eepd1, thereby exacerbating DNA damage in hepatocytes. Notably, Eepd1 liver-specific knockout mice exhibited aggravated hepatic DNA damage and further progression of NASH. To identify a therapeutic approach for CIH-induced NASH, we conducted a drug screening and found that Retigabine dihydrochloride suppressed CIH-mediated Eepd1 degradation, leading to alleviated DNA damage in hepatocytes. These findings imply that targeting CIH-mediated Eepd1 degradation could be an adjunctive approach in the treatment of NASH exacerbated by OSAS.

Short CV

Junli Liu, Professor of Endocrinology
Shanghai Jiaotong University School of Medicine
Shanghai Jiaotong University affiliated 6th People`s Hospital
Shanghai Diabetes Institute

Dr. Junli Liu has received the "National Overseas High-level Talents" and "National Science Fund for Excellent Young Scholars" awards, and he also serves as the part-time Chief Editor of Metabolism Open (ESCI, Elsevier). He received his Ph.D. from the Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences in 2009, under the supervision of Dr. Junyin Yuan (Harvard). He completed his postdoctoral training at MIT and Harvard Medical School. Dr. Liu's long-term research focuses on lipid and carbohydrate metabolism in the liver and adipose tissues, and their relationship with metabolic diseases. To date, Dr. Liu has published 21 papers in high-impact journals, including first author in Cell (3 papers) and additional papers as corresponding author in Cell Metabolism (2 papers), Science Translational Medicine, and Advanced Science. His research has been highlighted in 8 editorial reviews in prestigious journals such as Nature Medicine, with one paper recognized as an ESI Highly Cited Paper and another receiving "Most Picked Award" from Cell Press. Moreover, he was also invited to publish a highlight review (Voices) about his research findings in Cell Metabolism. Furthermore, Dr. Liu has obtained approval for one clinical trial, filed 10 patent applications, and been granted 2 patents.

Redox signaling in acute inflammation

Juan Sastre

Department of Physiology, Faculty of Pharmacy, University of Valencia, Spain

Email: juan.sastre@uv.es

Abstract

Acute inflammation is characterized by heat, erythema, pain, and swelling of the affected organ or tissue as well as by the respiratory burst of activated leukocytes. Acute pancreatitis has been studied in our lab as a model of acute inflammation. It is an inflammatory process of the pancreatic gland that eventually may lead to a systemic inflammatory response, and in severe cases to death by multiple organ failure. A key early event in pancreatic damage is glutathione depletion, which is transient in mild pancreatitis, but it is maintained over a long time in severe pancreatitis due to inefficient induction of glutamate cysteine ligase. In addition, there is blockade of the trans-sulfuration pathway due to nitration of cystathionine β-synthase. Interestingly, pancreatic inflammation is associated with protein cysteinylation, but not with glutathione oxidation or protein glutathionylation, leading to disulfide stress. Two types of targets of disulfide stress were identified: redox buffers, such as ribonuclease inhibitor or albumin; and redox-signaling thiols that include tyrosine and serine/threonine phosphatases, which markedly affect the inflammatory cascade. Protein cysteinylation is regulated by thioredoxin 1 and thioredoxin-related protein of 14 kDa (TRP14). The inflammatory cascade is also regulated by PGC-1α, which forms a complex with the NF-kB p65 subunit. This inhibitory complex markedly restrains specifically the up-regulation of interleukin 6 that triggers pulmonary inflammatory infiltrate and damage. Obesity causes marked PGC-1α deficiency in the pancreas promoting pulmonary damage. In the course of acute pancreatitis, p53 drives necroptosis of acinar cells via downregulation of sulfiredoxin and peroxiredoxin 3 and enhanced generation of mitochondrial reactive oxygen species. In conclusion, maintained glutathione depletion together with disulfide stress, PGC-1α deficiency, and p53-driven necroptosis decisively contribute to a severe outcome in acute inflammation.

Short CV

Juan Sastre is a Professor in Physiology at the University of Valencia, Spain. The most relevant scientific findings of his research group are related to oxidative stress and redox signaling in acute pancreatitis. He is currently President of European Society for Free Radical Research (SFRR-E) since January 2023. He was General Secretary of SFRR-E from 2013 till 2020. Juan Sastre has published > 150 articles, with currently > 11,000 citations, and an H-index of 58.

Oxidation and enzyme-mediated changes to the artery wall in cardiovascular disease

Michael J. Davies

Department of Biomedical Sciences, Panum Institute, University of Copenhagen, Denmark

Email: davies@sund.ku.dk

Abstract

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide. Atherosclerosis, a major underlying cause of CVD, is characterized by cholesterol and lipid accumulation in the artery wall and formation of plaques; these develop slowly and can be asymptomatic for decades. Destabilization and rupture of atherosclerotic plaques can be sudden and give rise to vascular occlusion and an acute myocardial infarction or stroke. Despite the importance of plaque stability, the mechanisms underlying rupture are poorly understood, though there is considerable evidence for extracellular matrix (ECM) alterations and a weakening of plaque structure. Compared to stable plaques, rupture-prone plaques typically contain higher levels of activated inflammatory cells that generate potent oxidants, such as hypochlorous acid and nitrating species which can both damage ECM proteins directly, or activate proteases that degrade ECM components.

In this presentation, data consistent with alterations to the nature and type of materials in plaque ECM will be presented, together with modifications to these materials, as determined by immunocytochemistry, immunoblotting and LC-MS/MS studies. Analysis of materials present in, or extracted from carotid plaques, has allowed identification of large numbers of differentially-abundant proteins between soft (rupture-prone) and hard (stable) plaques. Many of the overabundant proteins in soft plaques are involved in inflammation and ECM remodeling. LC-MS analyses have shown the presence of chlorinated, nitrated and oxidized species on ECM components, together with a marked increase in cleaved proteins, as judged by N-terminal proteomics, which allows detection of large numbers of cleaved peptides, consistent with extensive protein damage. The protein identities and the sites of cleavage have been characterized in some cases. These species are present at significantly higher abundance in unstable compared to stable plaques. These data offer a unique insight into the inflammatory and proteolytic mechanisms of plaque destabilization in CVD.

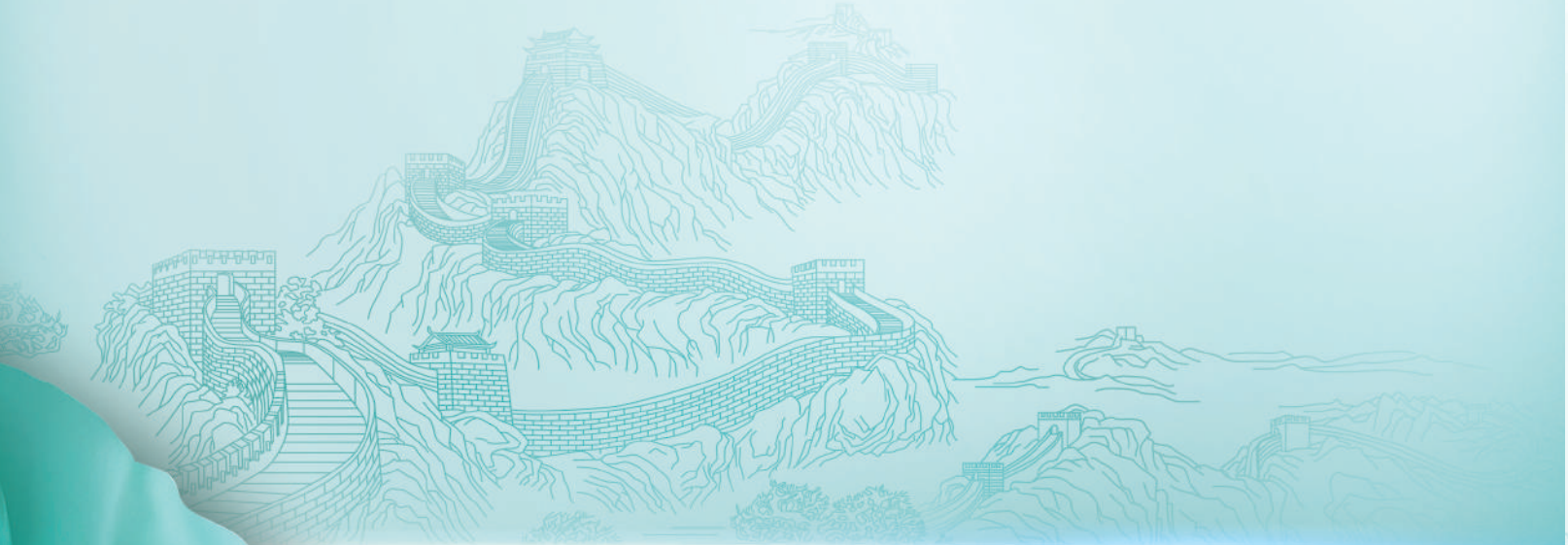
Key words: Atherosclerosis, Proteomics, Protein oxidation, Extracellular matrix, Myeloperoxidase, Peroxynitrite.

Short CV

Prof. Davies works at the University of Copenhagen, Denmark, and was previously Director of the Heart Research Institute, Sydney, Australia. He is joint Editor-in-Chief of 'Redox Biochemistry and Biology'. His research group is focused on the mechanisms and consequences of protein oxidation and extracellular matrix modification and in human disease and particularly cardiovascular pathologies.

Symposium-4(S4)

New approach for precision redox research



Chair: Xiangliang Yang (杨祥良)

Huazhong University of Science and Technology, China

Email: yangxl@hust.edu.cn

Short CV

He is the chair professor of the College of Life Science and Technology, Huazhong University of Science and Technology and the director of National Engineering Research Center for Nanomedicine. He is also the chief scientist of the "Nano Research" Project of the Major Scientific Research Program (973) and the leader of the Innovation Team for "Anti-tumor nanomedicine" in the key field of the Ministry of Science and Technology of China. Serving as vice-chairman in several key committees of national associations, including the Nanomedicine Committee of Chinese Pharmaceutical Association (CPA), the Nanomedicine Committee of China Anti-Cancer Association (CACA), the Nanomedicine and Engineering Committee of Chinese Society of Biomedical Engineering (CSBME). His research focuses on the fundamental study and clinical translation of nanomedicine. He has published over 480 peer-reviewed articles in Nature Nanotechnology, Nature Biomedical Engineering, Chemical Society Reviews, Nature Communications, Advanced Materials, etc, with over 20,000 citations and an H-index of 79, and has edited 3 books on nanomedicine and obtained 90 patents approved by NIPA of China. In addition, he has received several awards, including the first-tier prize of Science and Technology Progress Awards of Hubei Province of China. His research results in 4 approved new drug certificates, 17 drug registration approvals, 3 clinical approvals, and several products on the market.

Chair: Kwang Pyo Kim

Kyung Hee University, Korea

Email: kimkp@khu.ac.kr

Short CV

EDUCATION

University of Illinois at Chicago, Ph.D. Biochemistry, January, 2002.

Seoul National University, Korea, M.S. Chemistry, February, 1992.

Seoul National University, Korea, B.S. Chemistry, February, 1990.

EMPLOYMENT

Sep 2013-	Kyung Hee University Department of Applied Chemistry Professor
Mar 2013-Aug 2013	Konkuk University Department of Molecular Biotechnology, Professor
Mar 2004-Feb 2013	Konkuk University Department of Molecular Biotechnology, Assistant/Associate Professor
Jan 2002-Feb 2004	Harvard Medical School Dept of Cell Biology, Post-doctoral fellow (Research Advisor : Steven P. Gygi)

SELECTED PUBLICATIONS

1.Paraoxonase-2 agonist vutiglabridin promotes autophagy activation and mitochondrial function to alleviate non-alcoholic steatohepatitis. Shin GC, Lee HM, Kim N, Hur J, Yoo SK, Park YS, Park HS, Ryu D, Park MH, Park JH, Seo SU, Choi LS, Madsen MR, Feigh M, Kim KP, Kim KH. Br J Pharmacol. 2024 Jun 9. doi: 10.1111/bph.16438.

2.Enrichment and MALDI-TOF MS Analysis of Phosphoinositides in Brain Tissue. Le HT, Nguyen DPL, Jung GT, Kim E, Yang SH, Lee SM, Lee EA, Jung W, Kim TW, Kim KP. J Am Soc Mass Spectrom. 2024 Jun 5;35(6):1069-1075. doi: 10.1021/jasms.3c00364.

3.Constitutive activation mechanism of a class C GPCR. Shin J, Park J, Jeong J, Lam JH, Qiu X, Wu D, Kim K, Lee JY, Robinson CV, Hyun J, Katritch V, Kim KP, Cho Y. Nat Struct Mol Biol. 2024 Apr;31(4):678-687. doi: 10.1038/s41594-024-01224-7.

4.CREB-Regulated Transcriptional Coactivator 2 Proteome Landscape is Modulated by SREBF1. Lim JM, Anwar MA, Han HS, Koo SH, Kim KP. Mol Cell Proteomics. 2023 Aug 28;22(10):100637. doi: 10.1016/j.mcpro.2023.100637.

Fluorescence Imaging for the Progression of Oxidative Stress-Related Diseases

Bo Tang (唐波)

Laoshan Laboratory, China

Email: tangb@sdnu.edu.cn

Abstract

Oxidative stress is an imbalance between oxidation and antioxidant processes within an organism, which can lead to damage of biomacromolecules and become one of the important factors in aging and disease. During the process of oxidative stress, the levels of reactive molecules within cells fluctuate, closely correlated with the occurrence and development of diseases. Therefore, precise detection of these biomolecules has attracted wide attention. In response to their low concentrations, continuous changes, short half-lives, and characteristics of interaction and conversion, we have developed a series of novel fluorescent probes. We established a new method for ultra-high sensitivity, real-time in situ, dynamic, and simultaneous imaging of cellular reactive molecules (such as reactive oxygen species, enzymes, etc.), obtaining important information on the involvement of these reactive molecules in the oxidative stress process of organisms, as well as their regulation of the progression of cardiovascular diseases and brain diseases.

Key words: ROS; fluorescence imaging; biomacromolecules

Short CV

Bo Tang, director of the Department of Health Oceans and Sustainable Resource Utilization Research at Laoshan Laboratory, and professor at Shandong Normal University. He serves as a member of the Science and Technology Committee of the Ministry of Education, was nominated for the First National Outstanding Science and Technology Worker Award (the only one in Shandong Province), serves as the chief scientist of the 973 Program, is a recipient of the National Distinguished Young Scientists Fund, and is a national-level candidate of the New Century National Talent Project and the "Ten Thousand Talent Program" of the Thousand Talents Plan. The team he leads has been selected for the Ministry of Education's Changjiang Scholars and Innovative Team Development Plan, and is recognized as the Huang Danian-style Teacher Team at the national level, the first outstanding innovation team in Shandong Province, and an excellent innovation team of the Ministry of Science and Technology. He is primarily engaged in research on the synthesis of molecular and nanoscale fluorescent probes and their applications in biological imaging, as well as marine chemical biology and the high-value utilization of marine resources. He has led multiple national-level research projects, including the 973 Program, National Natural Science Foundation Key Projects, and major scientific instrument development projects. He has published over 400 SCI-indexed papers in journals such as Nat. Synth., Nat. Commun., Chem. Soc. Rev., J. Am. Chem. Soc., Angew. Chem. Int. Ed., Adv. Mater., with more than 43,000 citations. He has filed for over 80 national invention patents. As the principal investigator, he has been awarded one second prize of the National Natural Science Award, two second prizes of the National Science and Technology Progress Award, two first prizes of the Shandong Natural Science Award, two first prizes of the Shandong Science and Technology Progress Award, and one first prize of the Shandong Technological Invention Award.

Primate Phenotype and Genetic Analyses – From Basic Research to Clinical Applications

Yong-Gang Yao (姚永刚)

Kunming Institute of Zoology, Chinese Academy of Sciences, China

Email: yaoyg@mail.kiz.ac.cn

Abstract

Non-human primates (NHPs) have many advantages over other experimental animals in advancing biomedical research, especially the modeling of neurodegenerative and infectious diseases, and in understanding human beings, given the high degree of similarity in respect to genetics, anatomy, physiology, behavior, emotion, and cognitive function. NHPs constitute irreplaceable and in many ways superior models compared with common experimental animals such as rodents. Using NHPs to clarify the mechanisms underpinning genotypes and phenotypes will undoubtedly improve our understanding of complex traits and human diseases, as well as the responses of biological processes to environmental factors. On this point, NHPs constitute the perfect living template for us humans to understand ourselves. The establishment of the National Major Scientific and Technological Infrastructure for Primate Phenotype and Genetic Research provides researchers with a comprehensive and systematic platform that supports the translation from basic research to clinical applications. The creation of such facilities not only accelerates scientific research on primates but also offers new directions for addressing some of the challenges currently faced in life sciences and medical research.

Key words: Non-human primate, phenotype, genotype, clinical medicine, facility

Short CV

Dr. Yong-Gang Yao is the director general and principal investigator of the Kunming Institute of Zoology, Chinese Academy of Sciences (CAS). He obtained his bachelor's degree from Anhui Normal University in 1997 and his Ph.D. from the Kunming Institute of Zoology in 2003. He joined the School of Medicine at Johns Hopkins University as a post-doc in February 2003 and served as a visiting fellow at the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), in October 2004. He joined the Kunming Institute of Zoology as a principal investigator in December 2007.

Dr. Yao is involved in researching the genetic basis and molecular mechanisms underlying human diseases, with a particular focus on Alzheimer's disease. Furthermore, his team is also investigating the biology of the Chinese tree shrew, which is gaining prominence as a valuable laboratory animal. Currently, Dr. Yao is leading the establishment and construction of the National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility).

To date, Dr. Yao has published more than 300 peer-reviewed research articles and commentaries in various SCI-indexed journals, including Am J Hum Genet, PNAS, Autophagy, Alzheimers Dement, Natl Sci Rev, and Cell Discov. As of Auguest 30, 2024, his work has been cited over 11300 times (Web of Science), with an h-index of 54. He was recognized as one of the 2020-2023 ELSEVIER most-cited Chinese researchers. In addition to his research, Dr. Yao holds various editorial positions, including editor-in-chief of Zool Res and Zool Res Divers Conserv, associate editor of J Hum Genet, and editorial board member of J Genet Genomics and Mol Cell Neurobiol. He has received multiple awards, including the State Natural Science Award of China (second class) and Zhuliyuehua Award for Outstanding Teachers of the University of Chinese Academy of Sciences.

Quantitative metabolomics for redox biology and medicine

Huiru Tang (唐惠儒)
Fudan University, China
Email: huiru_tang@fudan.edu.cn

Abstract

Human metabonome contains more than 20 thousand metabolites with a huge concentration dynamic range, diverse properties, matrices and many different functions. Quantitative metabolomic analysis is essential for understanding the molecular aspects of mammalian biology, physiology and pathophysiology of various diseases hence redox biology and medicines. During last decades, metabolomics science has made huge progress in both technical and application areas. To achieve accurate quantitative metabolomic analysis, however, developing efficient novel analytical technologies remains to be one of the most urgent and extremely challenging tasks. NMR and MS are the dominant analytical tools with complementary information from them. This presentation will deal with the requirements of quantitative metabonomics and strategies to fulfill such tasks followed with some recent methodological advances. We will also discuss the major challenges metabolomic analysis is facing and possible strategies to overcome such problems with some important applications related to redox biology and medicines.

Key words: Quantitative metabolomics, elementomics, redox homeostasis

Short CV

Dr. Huiru Tang is a Distinguished Professor (metabonomics and systems biology) in Fudan University (School of Life Sciences and Zhangshan Hospital). He has been developing novel metabonomics methods and studying metabolic aspects of important diseases including obesity and complications as well as the symbiotic interactions between mammalian hosts and their gut microbiota for decades. After earned his PhD in chemistry from University of London in 1994, he worked at Institute of Food Research, UK, and Imperial College London as a Senior Scientist before joining the Chinese Academy of Sciences in 2005 as a professor. He joined Fudan University in 2014. He authored over 220 peer-reviewed papers with over 14000 citations (h-index: 67). He has been a Fellow of the Royal Society of Chemistry since 2005 and received an Award for Outstanding Young Scholars in 2008. He is now editorial board members (or Associated Editors) for numerous international scientific journals, and is the President of the Metabolomics Society of China.

Near-infrared xanthene dyes and *in vivo* ROS sensing

Youjun Yang (杨有军)

East China University of Science and Technology, China

Email: youjunyang@ecust.edu.cn

Abstract

Near-infrared light exhibits deep tissue penentration depth and is sought after for biomedical applications, i.e., intraoperative guidance, and photo dynamic therapy and more. The current gold standard is the indocyanine green (ICG) developed and approved in 1950s. ICG absorbs at 780 nm and is not stable chemically and photochemically. Development of bright and stable fluorophores absorbing and emitting beyond 800 nm is challenging.

In this presentation, our recent progress in development of near-infrared xanthenoid dyes (EC/ESi dyes) will be discussed. Briefly, benzannulation of xanthene scaffold is the key to redshift the spectral wavelengths and steric is the key to improves their resistance toward oxidation and bleaching. Currently, we have developed a series of EC/ESi dyes maximally absorbing at 740 nm, 780 nm, 820 nm, 835 nm, 860 nm, 880 nm, 920 nm, 1060 nm, and 1210 nm, respectively. Those dyes have the potentials for practical applications. Proof-of-concept biological *in vivo* imaging with mouse models will be presented. We further developed ROS-sensitive near-infrared fluorescent probes based on EC and ESi dyes. Their proof-of-concept *in vivo* applications were showcased with APAP-induced liver damages in mouse models.

Key words: Near-Infrared, Fluorescence, Redox, Sensing, *In vivo*

[1] J. Am. Chem. Soc., 2023, 145, 12013–12022.

[2] J. Am. Chem. Soc., 2022, 144, 14351–14362.

[3] Angew. Chem. Int. Ed. 2017, 56, 2979-2983.

[4] Angew. Chem. Int. Ed., 2024, e202402949.

[5] J. Am. Chem. Soc., 2022, 144, 2114-2119.

Short CV

Prof. Youjun Yang got his BS (2002) from University of Science and Technology of China and his PhD (2007) with Prof. Robert M. Strongin at Louisiana State University. Then, he joined the Anslyn group at the UT Austin as a postdoc. In 2010, he joined the faculty of the school of pharmacy, ECUST. His research falls within the area of dye chemistry. Current interests include NIR fluorescent dyes, molecular probes, photo-triggered drug release, and antibiotic xanthene dyes. He received the Czarnik Emerging Investigator Award (2018) and was supported by the NSFC Excellent Young Scientists program (2018).

Leucine 305 and 309 residues contribute to the formation of two human NRF2 bands in SDS-PAGE

Young-Sam Keum

College of Pharmacy, Dongguk University, Korea

Email: keum03@dongguk.edu

Abstract

Human NRF2 cDNA consists of 1,815 base pairs and encodes 605 amino acids. Therefore, human NRF2 is expected to appear around~65 KDa in SDS-PAGE based on the prediction of its molecular weight. However, human NRF2 appears around 110 KDa and exhibits two bands in SDS-PAGE. We have identified that leucine 305 and 309 residues existing in the Neh7 domain of human NRF2 are responsible for the formation of two bands in SDS-PAGE. While leucine 305 in primates is substituted into isoleucine in rodents, leucine 309 is conserved throughout the species. Moreover, we have identified that leucine 309 belongs to the LxxLL motif, which is essential for the binding to RXRα. We speculate that the intermolecular or intramolecular interaction of leucine 305 and 309 residues contributes to the formation of two bands of human NRF2 in SDS-PAGE.

Short CV

1991-2000 College of Pharmacy, Seoul National University, Korea (B.S. & M.S.)

2001-2007 Ernest Mario School of Pharmacy, Rutgers University, USA (Ph.D.)

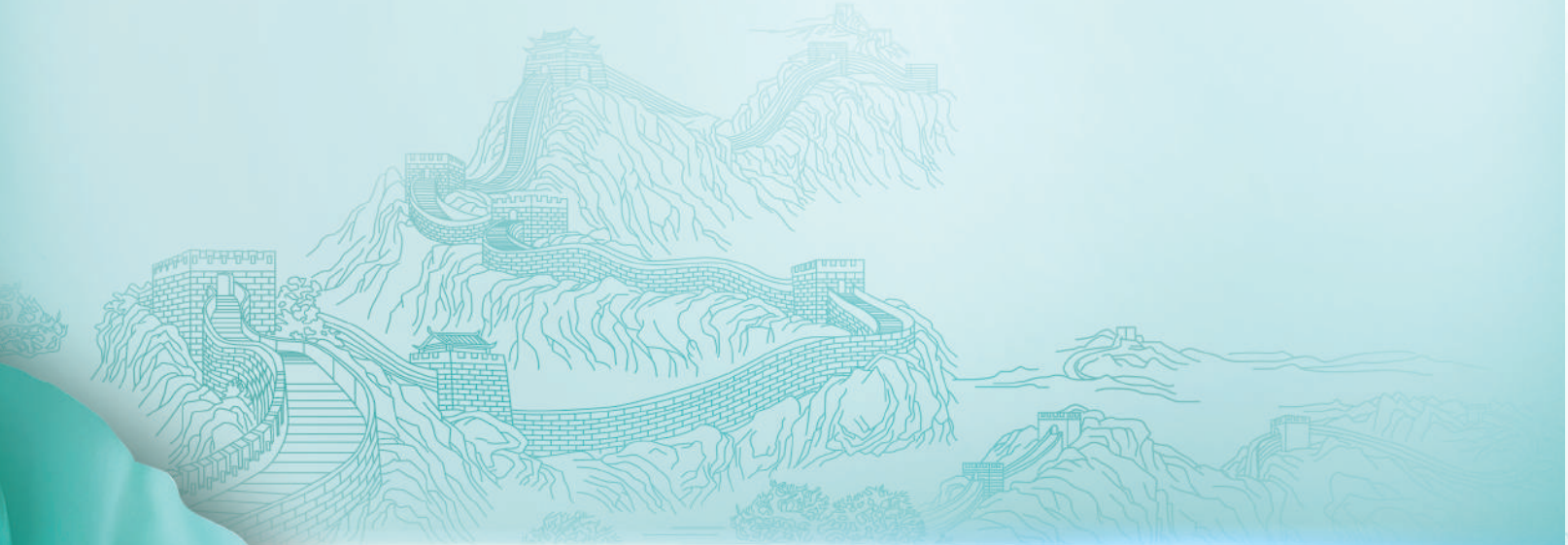
2007-2008 Post-doc, University of North Carolina at Chapel Hill, USA

2008-2010 Post-doc, The Hormel Institute, University of Minnesota, USA

2010-Present Professor, College of Pharmacy, Dongguk University, Korea

Symposium-5(S5)

Discovery of new molecules in redox network



Chair: Qiang Zhao (赵强)

College of Life Sciences, Nankai University, China

Email: qiangzhao@nankai.edu.cn

Short CV

Dr. Qiang Zhao received B. Eng degree from Northwestern Polytechnical University in 2001, and Ph.D. degree in Materials Science & Engineering from Tianjin University (China) in 2006. After three years of postdoctoral research at City University of Hong Kong, he joined College of Life Sciences, Nankai University (China) as associate professor in 2009, and was promoted to full professor in 2014. Dr. Zhao is the Director of Tianjin Key Laboratory of Bioactive Materials as well as the PI of State Key Laboratory of Medicinal Chemical Biology. He is the recipient of Distinguished Young Scientist Program of NSFC (2019) and Excellent Young Scientist Program of NSFC (2015). Currently his research interest focuses on biomaterials and regenerative medicine, including the development of novel biomaterials and therapeutic techniques for the treatment of cardiovascular diseases. He was awarded the First Class Prize of Natural Science Award of Tianjin (2019) as well as the Second Prize for Progress in Science and Technology of Tianjin (2016, 2021), and has authored over 100 peer-reviewed research papers (including Sci Transl Med, Nat Chem Biol, Nat Commun, Sci Adv, Cell Rep, Elife, Adv Mater, Circ Res, Adv Sci, J Am Soc Nephrol, Biomaterials, etc.), 6 book chapter, and >10 patents granted or pending.

NRF1 and NRF2 coordinate osteoclastogenesis and bone remodeling via ROS-dependent and independent mechanisms

Jingbo Pi (皮静波)

School of Public Health, China Medical University, China

Email: jbpi@cmu.edu.cn

Abstract

While nuclear factor erythroid 2-related factor 1 (NRF1, also known as NFE2L1) and its CNC-bZIP family member NRF2 transcriptionally coordinate multiple stress responses via regulating a variety of antioxidant and cytoprotective genes, they play distinct roles in maintaining various cell metabolism and function, including bone remodeling and homeostasis. In the present study, we aimed to understand the molecular mechanisms underlying osteoporosis induced by aging, estrogen deficiency and various environmental stresses, focusing mainly on the roles of NRF1 and NRF2 in osteoclastogenesis. By employing a candidate gene associate study using the UK biobank cohort we found that multiple variants of human NFE2L1 gene are associated with heel bone mineral density. Knockout of all isoforms of Nfe2l1 transcripts specifically in the myeloid cell lineage in mice resulted in increased osteoclast number and activity, decreased bone mass and accelerated bone loss induced by ovariectomy and aging. Mechanistic investigations using bone marrow-derived osteoclast progenitor cells and RAW 264.7 cells revealed that deficiency of Nfe2l1 leads to accelerated and elevated osteoclastogenesis, which is attributed to enhanced expression of Nfatc1/α, a master regulator of osteoclast differentiation. Further studies postulated a new mechanism that NRF1 functions as a key factor controlling the transcription of Nfatc1/α and osteoclast differentiation in an isoform-specific manner. Specifically, long isoforms of NRF1 (L-NRF1) positively regulates the transcription of Nfatc1/α and promotes osteoclast differentiation, whereas the short isoform NRF1-453 competes with L-NRF1 for the same DNA binding site(s) to suppress the transcription of Nfatc1/α, highlighting that NRF1 is crucial in fine-tuning osteoclastogenesis and thus bone homeostasis. In contrast, ablation of Nrf2 globally or myeloid-specifically in mice resulted in a relatively minor phenotype in bone metabolism under non-stressed condition, but exacerbated osteoclast activation and bone loss induced by prolonged exposure to multiple environmental oxidative stressors, including cadmium (Cd) and arsenic, suggesting that NRF2-dependent osteoclast homeostasis plays a crucial role against the oxidative stressors-induced osteoclast overactivation and osteoporosis. Mechanistic in vitro studies revealed that Nrf2 deficiency aggravates the osteoclast differentiation provoked by low levels of Cd exposure, in which ROS-mediated L-NRF1 activation plays a crucial role in coordinating Nfatc1/α expression, osteoclastogenesis and thus bone remodeling and homeostasis. Together, NRF1 and NRF2 coordinatively respond to environmental oxidative stress and orchestrate osteoclastogenesis and bone remodeling. Mismatched and/or imbalanced activation of L-NRF1 and NRF2 in response to environmental cues may disrupt redox-sensitive signaling leading to impaired bone metabolism and function, bone remodeling in particular.

Key words: NFE2L1, osteoclast, NFATc1, osteoporosis, NRF2

Short CV

Jingbo Pi, MD, Ph.D.

Dr. Pi received M.D. (1990) and M.S. on Occupational Health (1995) from China Medical University, and Ph.D. in Medical Sciences from The University of Tsukuba, Japan in 2002. He had postdoctoral training at NIEHS, USA (2002-2004) and The Hamner Institutes for Health Sciences, USA (2004-2006). He worked as a Research Investigator, Assistant Investigator and Associate Investigator at The Hamner Institutes for Health Sciences (2006-2013). In 2013, Dr. Pi was recruited as a professor of China Medical University, and since then he has been serving as the Dean of School of Public Health. In 2008, Dr. Pi received the Outstanding New Environmental Scientist (ONES) Award, NIEHS, USA. Dr. Pi's research focus is on environmental oxidative stress and metabolic disorders. His research has been funded by NIDDK (USA), NIEHS (USA), Nature Science Foundation of China and the Ministry of Science and Technology, China. He has authored/co-authored over 200 peer-reviewed papers/book chapters with more than 10,000 citations. Dr. Pi has served as a board member and president/vice president of Stem Cell Specialty Section, SOT, USA and an advisor and subgroup co-chair of IARC/WHO Monographs. Currently, he is an Associate Editor of Toxicology and Applied Pharmacology and Toxicology Reports, and also serves as vice president of multiple Specialty Sections of Chinese SOT. In addition, he functions as the director of the Key Laboratory of Environmental Stress and Chronic Disease Control and Prevention, Ministry of Education, China.

HSF1 regulates nuclear/cytoplasmic and mitochondrial proteotoxic stress responses

Akira Nakai

Institution, Country Yamaguchi University Graduate School of Medicine, Japan

Email: anakai@yamaguchi-u.ac.jp

Abstract

Dysregulation of protein homeostasis (proteostasis) in different organelles is associated with age-related diseases including neurodegenerative disease and cancer. To cope with proteotoxic stresses, cells are equipped with adaptive mechanisms called proteotoxic stress response (PSR). Among these, the heat shock response (HSR) is evolutionarily conserved and is characterized by the induction of heat shock proteins (HSPs), which assist protein folding. HSR is regulated by heat shock transcription factor 1 (HSF1) in human cells and maintains proteotoxic capacity in the nucleus and cytoplasm. We recently showed that HSF1 also regulates mitochondrial unfolded protein response (UPRmt) and maintains mitochondrial function, which is related with redox homeostasis. To understand regulatory mechanisms of HSR, we have been studying regulation of HSF1-transcriptional complexes under proteotoxic stress conditions. I introduce mechanisms of heat shock gene transcription involving the stress-induced HSF1 complex formation and changes in chromatin states and show that aberrant regulation of these mechanisms is associated with cancer progression.

Key words: heat shock, proteostasis, mitochondria, transcriptional complex, cancer

Short CV

1981-1987 Undergraduate at Tottori University School of Medicine, Japan;

1987-1991 Graduate at Tottori University;

1991-1993 Northwestern University, IL, USA, Postdoctoral fellow;

1993-1998 Chest Disease Research Institute, Kyoto University, Assistant Professor;

1998-2000 Institute for Frontier Medical Sciences, Kyoto University, Assistant Professor;

2000-present, Yamaguchi University School of Medicine, Professor.

Grasip the void of Redox
——the new relic of Tissue Bank

Bo Xie (谢波)

Shanghai Tissuebank Biotechnology Co., Ltd

Email: xiebo@catb.org.cn

Abstract

Oxidative stress plays a critical role in the development and progression of various diseases, including cancer, aging, and metabolic disorders. Our team leverages a multi-omics platform, integrating proteomics, metabolomics, and genomics, to investigate the molecular mechanisms of oxidative stress, particularly its regulatory roles in specific disease models. Studies have shown that oxidative stress responses at the metabolic level differ among individuals, especially in energy metabolism pathways in insulin-resistant subjects, highlighting new avenues for personalized therapeutic strategies.

Our team members previously contributed to a study on metformin, which revealed the mechanism by which physiological concentrations of metformin activate AMPK through a lysosomal pathway. High concentrations of metformin inhibit mitochondrial activity and increase intracellular AMP levels, while physiological doses activate AMPK via a receptor-mediated pathway. The study also demonstrated that metformin regulates ROS (reactive oxygen species) in a dose-dependent manner, either reducing or increasing ROS levels, underscoring its dual-edged role. This finding provides new insights for further exploration of metformin's regulation of redox homeostasis.

Currently, our team is investigating the potential of N-acetylcysteine (NAC) in improving poor engraftment following hematopoietic stem cell transplantation. Preliminary results indicate that NAC enhances hematopoietic stem cell function by scavenging excess ROS in the bone marrow, promoting endothelial progenitor cell regeneration, and alleviating platelet engraftment delays.

In the future, we plan to build upon the findings of metformin's systemic regulation of ROS, integrating multi-omics and pharmacokinetics research to explore its mechanisms in various organs, tissues, and specific cell types. By combining multi-omics data, we aim to elucidate its impact on redox homeostasis and construct a network of cell fate regulation to advance research in disease diagnosis and treatment. Additionally, we will expand the application of our multi-omics platform to investigate the potential mechanisms of redox regulation in other diseases, further uncovering its role in various pathological processes. Through this platform, we aim to translate these research findings into clinical applications and actively seek collaboration with experts from other fields to foster innovation in clinical practice and disease research.

Structural library and visualization of endogenously oxidized lipids

Ken-ichi Yamada

Department of Molecular Pathobiology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka, 8128582, Japan

Email: kenyamada@phar.kyushu-u.ac.jp

Abstract

Recently, oxidized phospholipids have been reported to be involved in various diseases. For example, lipid peroxides induce a new cell death form, "ferroptosis," and epoxidized ω3 fatty acids, an oxidized metabolite, are engaged in worsening allergies. In addition, the complex between lipid peroxide-derived aldehyde and protein is involved in angiogenesis. Thus, although the importance of oxidized phospholipids is widely recognized in the induction of inflammation and cell death, the number of oxidized phospholipids available or detectable is limited. This lower number would be due to the lack of appropriate detection techniques.

Here, we have developed a fluorescent probe to detect "lipid-derived radicals," key molecules during the chain reaction of lipid peroxidation. Furthermore, since this probe can covalently bind to lipid-derived radicals, we have constructed an LC/FL/HRMS/MS system and have successfully analyzed the structures of 132 lipid-derived radical species1). In addition, the involvement of lipid-derived radicals in the vitamin K cycle has been clarified recently.

Next, a non-targeted analysis of phosphatidylcholine-derived oxidized lipids (oxPCs) was performed using a high-resolution mass spectrometer, and a library of 465 oxPCs was constructed 2). Furthermore, we detected 70 kinds of oxPCs in mice with acetaminophen-induced acute liver failure, and mass imaging of oxidized lipids was successfully performed.

In this symposium, I would like to introduce our recent research, including the detection and structural analysis of oxidized phospholipids and their application using animal models.

<Yamada K, et al. Nat Chem Biol. 2016; 12:608-613. Matsuoka Y, et al. Nat Commun. 2021; 12:6339.>

Key words: Lipid radicals, Oxidized Phospholipids

Short CV

Ken-ichi Yamada is a Professor at the Faculty of Pharmaceutical Sciences, Kyushu University, Japan. He studied ESR and MRI imaging at Kyushu University and received his Ph.D. in Pharmaceutical Sciences from the Faculty of Pharmaceutical Sciences, Kyushu University, Japan. He did his postdoctoral work at NCI/NIH, USA, for two years, working on magnetic resonance imaging and radiation biology. Specific interests in Yamada's lab include the detection and regulation of oxidized lipids.

Regulation of protein-protein interactions as a new paradigm in drug discovery: Targeting the oncogenic role of E74 Like ETS transcription factor 3 (ELF3) through modulation of its protein-protein interaction

Youngjoo Kwon

Graduate School of Pharmaceutical Sciences, College of Pharmacy, Ewha Womans University, Seoul, 03760, Korea

Email: ykwon@ewha.ac.kr

Abstract

Protein-protein interactions (PPIs) form intricate networks essential for maintaining homeostasis under normal physiological conditions. Dysregulated PPIs are often implicated in the pathogenesis of various diseases, making them critical targets in drug discovery. However, disrupting these dysregulated PPIs remains challenging due to the large and shallow nature of PPI interfaces, which typically lack well-defined binding sites.

While some protein or peptide-based PPI inhibitors have been developed, their clinical utility is limited by drawbacks such as poor cellular internalization, low bioavailability, and high immunogenicity. Consequently, there is an ongoing effort to identify small molecule PPI regulators capable of binding to PPI interfaces with high specificity and affinity. Despite these efforts, only a limited number of small molecule PPI modulators have advanced to clinical use.

In our research, we have focused on developing small molecule modulators for specific PPIs by identifying 'hotspots'—small regions within PPI interfaces that are primarily responsible for the binding affinity between two proteins. Using a comprehensive approach that combines biochemical and analytical techniques with in silico structural studies, we have successfully identified small molecule inhibitors targeting these PPI hotspots. We have also elucidated their mechanisms of action and demonstrated their anticancer efficacy both in vitro and *in vivo*.

Short CV

2005.3-presnt: Assistant Professor, Associate Professor, and Professor, College of Pharmacy & Graduate School of Pharmaceutical Sciences, Ewha Womans University

2021.7- 2027.2: Director, Ewha Drug Development Research Core Center

2021.8- 2023.7: Chairman, Graduate School of Pharmaceutical Sciences, Ewha Womans University

2017.8- 2019.7: Associate Dean, College of Pharmacy, Ewha Womans University

2019: Director, Division of Pharmaceutical Analysis, Pharmaceutical Society of Korea

2023- 2025: Korea Drug Development Fund (KDDF), Investment Review Committe

Symposium-6(S6)

Redox modification of biomacromolecules

Chair: Zhonghong Gao (高中洪)

Huazhong University of Science and Technology, China

Email: zhgao144@hust.edu.cn

Short CV

1998, PhD of Huazhong University of Science & technology; 2000, associate professor of Huazhong University of Science & technology; 2001.9.-2002.8., visiting scientist in The University of Texas, Medical School at Houston, U.S.A; 2004, professor of Huazhong University of Science & technology

Research interests

Extraction, identification, bioactivities (particularly on anti-oxidative and anti-nitrative activities) of nature products; the mechanism and the cellular effects of the redox-based post-translational modification of proteins, particularly on protein oxidation and tyrosine nitration; nanotoxicology based on oxidative stress. As first author or corresponding author, professor Gao published more than 60 papers on peer reviewed international journals, and these papers have got more than 2500 citations.

Biology and pharmaceutical development of S-nitrosylation

Lee Jia (贾力)

Minjiang University; LeeChen Biotech & Pharmaceuticals, China

Email: 2697270856@qq.com

Abstract

There are several approaches to delivering exogenous NO for the regulation of neuronal and cardiovascular functions. S-nitrosylation technology involves the covalent attachment of an NO group to the thiol group (-SH) of a cysteine residue in a protein, forming an S-nitrosothiol (SNO). This reaction can occur enzymatically, non-enzymatically, or be catalyzed by metal centers. Reversible S-nitrosylation of protein Cysteine residues has emerged as an important post-translational modification across a wide variety of living organisms, from bacteria to mammals, resulting in NO-like bioactivity.

We have synthesized and developed S-nitrosylated captopril (CapNO), a compound with significant pharmaceutical potential. Due to the inherent instability of the S-NO bond in CapNO, its solid form had never been successfully obtained before. Here, we present groundbreaking evidence that we are the first to synthesize CapNO crystals and formulate them as a cyclodextrin inclusion complex. By incorporating a single water molecule within the molecular structure, we stabilized the S-NO bond through ionic binding. The cyclodextrin inclusion complex further enhanced stability by providing spatial steric hindrance, protecting the vulnerable S-NO bond from degradation. This innovative approach overcomes the technical challenges of producing large quantities of stable CapNO crystals for pharmaceutical use. We have thoroughly characterized the physicochemical properties of CapNO.

Intravenous administration of CapNO in rats resulted in increased cerebral and vascular blood flow, along with an acute reduction in mean arterial pressure. In rats with acute hypertension induced by an iNOS inhibitor, CapNO significantly counteracted the hypertensive effects. Bolus injections of CapNO into the left atrium of awake dogs produced immediate epicardial vasodilation, increased coronary diameter and blood flow, a transient decrease in aortic pressure, and a transient increase in heart rate and left ventricular dP/dt. In contrast, intravenous administration of captopril alone did not produce these effects.

Subchronic treatment of spontaneous hypertensive rats (SHR), Dahl salt-sensitive hypertensive rats (SS/Jr), and two-kidney, one-clip Goldblatt hypertensive rats with oral CapNO significantly reduced mean arterial

pressure to normotensive levels without adverse effects on blood chemistry or hematology tests. Based on these results, the no observed adverse effect level (NOAEL) for CapNO can be safely established at 100 mg/kg/day. CapNO, which combines the properties of a nitric oxide donor and an angiotensin-converting enzyme (ACE) inhibitor, shows promise for beneficial effects on both the neuronal and cardiovascular systems.

Key words: NO, S-nitrosylation, cardiovascular effects

Short CV

Dr. Jia is well known for his pioneering research on 1) Nitric oxide (NO) and S-nitrosylation molecular biology and pharmaceutical innovation; 2) Cancer metastasis chemoprevention that prevents circulating tumor cells (CTCs) from germination into metastatic niches, and thus eliminating the root cause of cancer metastasis; 3) Innovative bionanomaterials used for molecular delivery, biosensing and precisely targeting blood CTCs; and 4) Biochemical basis of nutraceuticals used for long-term prevention and treatments of major diseases.

Jia received his Ph.D. in 1994 from the State University of New York, USA, advised by Robert Furchgott (the 1998 Nobel Laureate). He joined the prestigious National Cancer Institute/NIH, USA, at the tenure position (GS14/9) managing 6.3 millions of pharmacological contract research before recruited by "The China Recruitment Program of Global Experts". He then holds the rank of Distinguished Professor at the Fuzhou University and the Minjiang University, China, respectively. He is a Fellow of American Association of Pharmaceutical Scientists (AAPS; 2011) and a Section Chair of the AAPS (2009-2012), a Member of the International Eurasian Academy of Sciences (IEAS; 2020), and a Member-at-Large of the Chinese Chemical Society (2021), the Founding Chair of the Intelligent Functional Pharmaceutics Section of Chinese Pharmaceutical Association (CPA; 2021-) and the Council Member of CPA. He is the Associates Editor for Current Drug Metabolism, and for Drug Metabolism and Bioanalysis Letters (2023-), as well as Editors for other four Journals. He received many prestigious awards and recognitions. He dedicates to translating scientific discoveries into unmet needs of major diseases. He led teams to developing 3 candidate molecules for clinical trials. His 240+ publications are highly relevant to molecular biology and translational research with citations >16700, h-index 62 and i10-index 191 (Google scholar). He has collaborated with scientists from Switzerland, Sweden, Russia, the USA, the UK, Australia, South African.

Lipid Peroxidation and Cardiovascular Disease

Huiyong Yin (尹慧勇)
City University of Hong Kong, China
Email: huiyoyin@cityu.edu.hk

Abstract

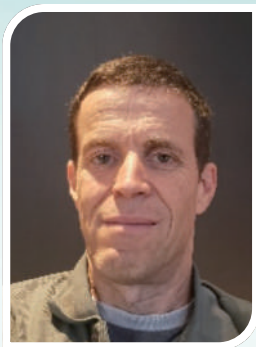
Background: As an iron-dependent form of regulated cell death caused by lipid peroxidation, ferroptosis has been implicated in ischemic injury but the underlying mechanisms in acute myocardial infarction (AMI) remain poorly defined. Acetaldehyde dehydrogenase 2 (ALDH2) catalyzes detoxification of lipid aldehydes derived from lipid peroxidation and acetaldehydes from alcohol consumption. The Glu504Lys polymorphism of ALDH2 (rs671, ALDH2 *2), affecting around 8% world population and 40% East Asians, is associated with increased risk of MI. This study aims to investigate the role of ALDH2 and ferroptosis in MI. Methods: A Chinese cohort of 177 acute heart failure patients with ALDH2 and ALDH2*2 were enrolled. MI mouse model of left anterior descending coronary artery ligation (LAD) was conducted on wild type, ALDH2*2, and mice with cardiomyocyte-specific knock down of eukaryotic translation initiation factor 3 subunit E (eIF3E) by adeno-associated virus. Lipid peroxidation products were measured by mass spectrometry-based lipidomics and metabolomics in human plasma and in mouse serum and heart tissues. Results: Human ALDH2 *2 carriers exhibit more severe heart failure post-AMI with features of ferroptosis in blood samples in lipidomic analysis, including increased levels of multiple classes of oxidized phospholipids, serum heme, and decreased levels of antioxidants, such as Coenzyme Q-10 (Co-Q10) and tetrahydrobiopterin (BH4). Similar features were observed in MI mouse models of ALDH2 *2, whereas ferroptosis inhibition by Fer-1 significantly improved heart functions and reversed ferroptosis markers. Importantly, ALDH2*2 led to significantly decreased protein levels of ALDH2, whereas ferroptosis related proteins including Transferrin receptor (TFRC), Acyl-CoA synthetase long chain family member 4 (ACSL4), and Heme oxygenase 1 (HMOX1) were upregulated specifically in the infarct heart tissues. Mechanistically, ALDH2 physically interacted with eIF3E to modulate translation of critical proteins involved in ferroptosis, and ALDH2 deficiency in ALDH2 *2 mutant predisposes cardiomyocytes to ferroptosis by promoting Tfrc/Acsl4/Hmox1 translation. Consistently, cardiomyocytes-specific eIF3E knock down restored ALDH2 *2 cardiac function by attenuating ferroptosis in MI. Conclusions: ALDH2 *2 aggravates acute heart failure in MI through promoting cardiomyocytes ferroptosis, and targeting

ferroptosis may be a potential therapeutic target for treating AMI, especially for ALDH2 *2 carriers.

Key words: Lipid peroxidation, Ferroptosis, Myocardial Infarction

Short CV

Dr. Huiyong YIN is a tenured Professor in the Department of Biological Sciences and Associate Dean (Research) of the Jockey Club College of Veterinary Medicine and Life Sciences at City University of Hong Kong. He also serves as the Associate Dean for Research for JCC and Chair of College Research Committee. Before joining CityU, Prof. Yin was the Distinguished Principal Investigator and Group Leader of Lipid Metabolism in Human Nutrition-related Diseases at Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences, Shanghai, China. He was also the Distinguished Adjunct Professor in School of Life Sciences and Technology in ShanghaiTech University since 2013. Prof. YIN is one of the leading scientists in the field of redox regulation of glucose and lipid metabolism in human metabolic diseases including atherosclerosis, liver cancer, hyperuricemia and gout (http://www.cityu.edu.hk/bms/profile/huiyongyin.htm). He has published over 170 manuscripts in SCI journals, including Science, Nature, Cell Metabolism, Nature Cancer, JACS, Hepatology, JCI, Redox Biology, with > 14,600 citations and H-index of 66 (Google Scholar, Sept. 2024). He has been listed as the top 2% of the Most-Cited Scientists in the world by Stanford University and was awarded prestigious "Senior International Scientists" in 2021 by Chinese National Natural Science Foundation (NSFC).



The dynamic thiol redox proteome of macrophages and its role in the response to oxidative-inflammatory stress

Moran Benhar

Faculty of Medicine, Technion, Israel

Email: benhar@technion.ac.il

Abstract

Oxidative modifications of protein cysteine thiols regulate various physiological processes, including innate immune and inflammatory responses. We conducted proteomic and mechanistic studies to investigate the roles of protein thiol oxidation in inflammatory macrophages. Through these studies we uncovered new roles for thioredoxin in regulating the macrophage inflammatory response. We further characterized new thiol redox switches that regulate glutathione homeostasis and autophagy in activated macrophages. Overall, these studies have yielded new insights into the dynamic redox proteome of macrophages and the mechanisms by which macrophages adapt and fine-tune their responses according to a changing inflammatory and redox environment.

We next aimed to characterize how reactive sulfur species (RSS) and thiol persulidation influences macrophage oxidative-inflammatory response. We revealed that classical activation of mouse or human macrophages using lipopolysaccharide and interferon-γ (LPS/IFN-γ) triggers substantial production of RSS, leading to widespread protein persulfidation. Additional analyses revealed that this upsurge in cellular S-persulfidation engaged ~2% of total thiols and modified over 800 functionally diverse proteins, while in comparison the global proteome exhibited little changes. In this setting, S-persulfidation was largely dependent on the cystine importer xCT and the hydrogen sulfide-generating enzyme cystathionine γ-lyase. We further investigated the role of the sulfide-oxidizing enzyme sulfide quinone oxidoreductase (SQOR), and found that it acts as a negative regulator of S-persulfidation. Elevated S-persulfidation following LPS/IFN-γ stimulation or SQOR inhibition was associated with increased resistance to oxidative stress. Upregulation of persulfides also inhibited the activation of the macrophage NLRP3 inflammasome and provided protection against inflammatory cell death. These findings provide a better understanding of the effects of RSS in macrophages and highlight the crucial role of persulfides in enabling macrophages to cope with oxidative-inflammatory stress.

Key words: Redox Biology, Reactive Oxygen Species

Short CV

Dr. Benhar received his undergraduate degree in chemistry and graduate degree in biochemistry at the Hebrew University of Jerusalem, Israel. After a postdoctoral training at Duke University (USA) he joined in 2009 the Department of Biochemistry at the Technion-Israel Institute of Technology, as an Assistant Professor. In 2016 he became an Associate Professor at the Technion.

Dr. Benhar has a longstanding interest in oxidant signaling and in redox mechanisms involved in inflammation and cancer. Dr. Benhar and his group employ proteomic and biochemical tools to explore the roles of oxidative protein modifications in cellular signaling in macrophages and cancer cells. Research by Dr. Benhar has provided new insights into the crosstalk between nitric oxide and the thioredoxin antioxidant system in tumor and immune cells. His recent work revealed new roles and mechanisms by which of reactive sulfur species regulate inflammatory and cell death responses.

Immune memory against toxic aldehydes

Koji Uchida

Laboratory of Food Chemistry, Department of Applied Biological Chemistry, Graduate School of Agricultural and Life Sciences, The University of Tokyo, Tokyo 113-8657, Japan

Email: a-uchida@g.ecc.u-tokyo.ac.jp

Abstract

Natural antibodies, predominantly IgM, play an important role in the defense against pathogens and in maintaining homeostasis against oxidized molecules known as oxidation-specific epitopes. Due to the complexity of oxidized products, very few individual epitopes have been characterized in detail. Based on the fact that the B cell repertoire contains cells producing IgM against oxidation-specific epitopes, we investigated the presence of innate B cells that respond to modified proteins with aldehydes. Among the aldehyde associated with lipid peroxidation, acrolein, the most reactive of all aldehydes, was shown to be as a potential source of the innate epitopes. We also established the presence of innate B-1 cells that specifically respond to the acrolein-modified proteins via a B cell receptor-dependent mechanism. The V-D-J gene usage of the VH and VL for the anti-acrolein IgM-producing hybridoma was 100% identical to the germline gene sequences, suggesting clonal expansion of IgM-producing B cell population. Our discovery of acrolein as a source of innate epitopes suggests that, besides our common concept of aldehydes as toxic molecules, they may also play a role as a crucial signal for cell survival (also called a tonic signal) mediating the homeostatic responses via binding to proteins.

Key words: Innate immunity, innate antigens, aldehydes, covalent modification of proteins

Short CV

Professor Uchida received his Ph.D. from Nagoya University in 1988 and immediately became Assistant Professor at the same institution. After completing his postdoctoral training at the N.I.H. in Bethesda from 1990 to 1992, he was promoted to Associate Professor in the Laboratory of Food and Biodynamics, Nagoya University in 1996 and to Professor in 2011. Currently, he is a professor at the Laboratory of Food Chemistry, Graduate School of Agricultural and Life Sciences, The University of Tokyo.

A protein protein interaction between SOD1 and YWHAZ and YWHAE

Xin Gen Lei

[1] Department of Animal Science, Cornell University, Ithaca, NY 14853, USA

[2] Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853, USA

Email: xl20@cornell.edu

Abstract

Background: Copper-zinc superoxide dismutase 1 (SOD1) is one of the major intracellular redox enzymes in scavenging superoxide radicals. Past research has been focused on that type of antioxidant protection of the enzyme.

Objective and methods: The current study was conducted to explore its non-canonical role and the metabolic implications. We applied protein complementation assay (PCA) and revealed novel protein-protein interactions (PPIs) between SOD1 and tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein zeta (YWHAZ) or epsilon (YWHAE). We also used site-directed mutagenesis of SOD1 to characterize the binding conditions of the two PPIs. We also determined impacts of the PPIs' on lipid metabolism and cell growth and survival of HEK293T and HepG2 cells

Results and Discussion: The formation of the SOD1 and YWHAE or YWHAZ protein complex elevated enzyme activity of purified SOD1 in vitro by 40% ($P < 0.05$) and protein stability of over-expressed intracellular YWHAE (18%, $P < 0.01$) and YWHAZ (14%, $P < 0.05$). Metabolically, these PPIs were associated with lipolysis, cell growth, and cell survival in HEK293T or HepG2 cells. In conclusion, our findings unveiled two new PPIs between SOD1 and YWHAE or YWHAZ and their structural dependence, responses to redox status, mutual impacts on the enzyme function and protein degradation, and metabolic implications. Overall, revealing the unorthodox role of SOD1 will provide new perspectives and insights for diagnosing and treating diseases related to this and other antioxidant proteins.

Reference: Z. Q. Sun and X. G. Lei. 2023. Evidence and metabolic implications for a new non-canonical role of Cu-Zn superoxide dismutase. Int. J. Mol. Sci. 24(4), 3230; https://doi.org /10.3390/ijms24043230.

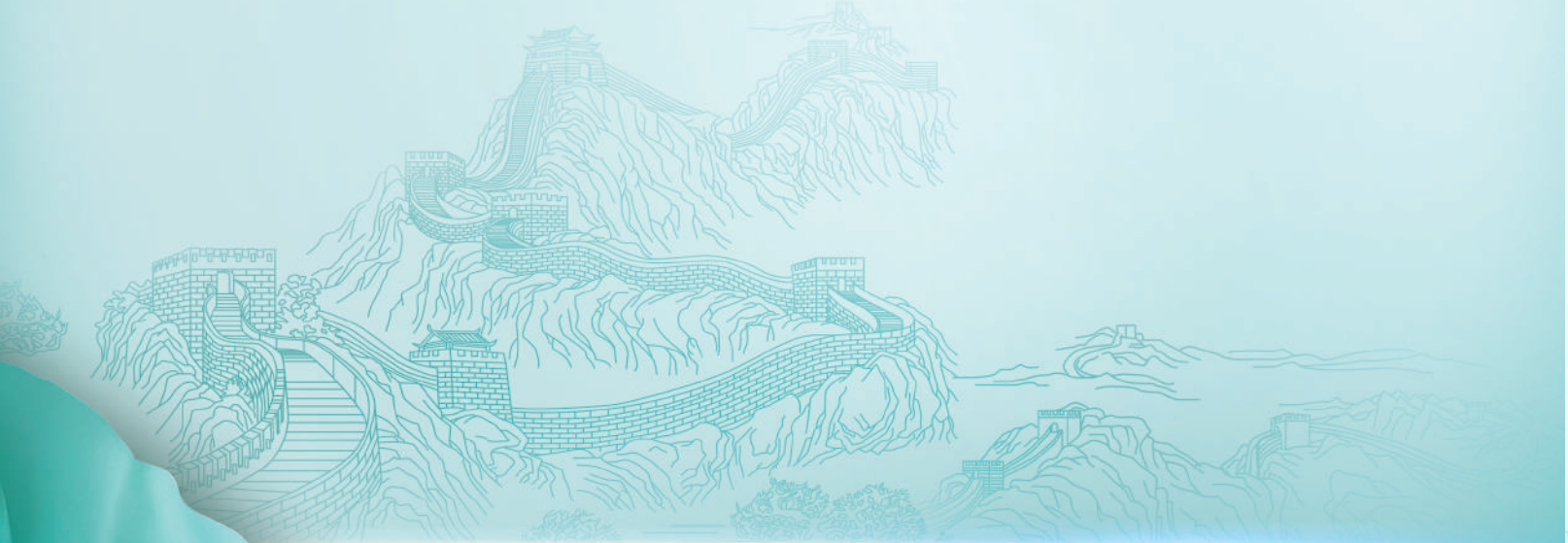
Key words: Antioxidant enzyme, non-canonical role, tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein

Short CV

Xingen Lei is a Professor of Molecular Nutrition at Cornell University. He has developed a new generation of bacterial phytases that are used by the feed industry in 50 countries. Lei also pioneered nutritional genomics of selenium in animals and revealed dual roles of selenium in oxidative stress and diabetes. Lei is an international leader in applying agriculture to prevent "hidden hunger". He currently serves as the Editor-in-Chief of The Journal of Nutrition, President of Trace Elements in Man and Animals, and Associate Dean of Research and Innovation in College of Agricultural and Life Sciences at Cornell University. Lei was elected as a Fellow of the National Academy of Inventors in 2021.

Symposium-YIO-1 (Y-1)

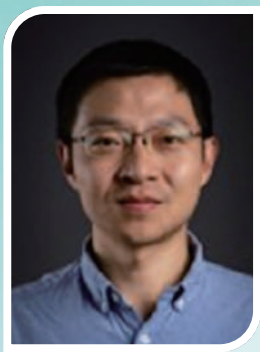
Redox modification of biomacromolecules
Redox and obesity, vascular function and metabolism



Chair: Li Xu (徐力)
Jilin University, China
Email: xuli@jlu.edu.cn

Short CV

Prof. Xu received her Ph.D. from Jilin University in 2002. She is currently a professor at the Key Laboratory of Molecular Enzyme Engineering, Ministry of Education, College of Life Sciences, Jilin University. From 2004 to 2005, she studied abroad as a national public scholarship visiting scholar at the INRA Institute in France. From November 2010 to March 2011, she was invited to serve as a visiting professor at Kwansei Gakuin University in Japan, where he conducted lectures and academic exchanges. From November 2012 to March 2013, she engaged in collaborative exchanges as a national public senior research scholar at George Washington University in the United States. Her research focuses on Nanomedicine: 1. Enhanced Targeted Nanocarrier for Hydrophobic Drug Delivery; 2. Designing a special functionalized nanozyme that depends on the interface effect of an inorganic nanocrystal. 3. Modification and assembly of nanoparticles with peptides and their applications in biotechnology. 4. Development of functional bioactive peptides in disease therapy.



Activation mechanism of phagocyte NADPH oxidase

Lei Chen (陈雷)

Peking University, China

Email: chenlei2016@pku.edu.cn

Abstract

Phagocyte NADPH oxidase, known as the NOX2-p22 complex, is responsible for transferring electrons from intracellular NADPH to extracellular oxygen. This process generates superoxide anions that are vital for killing pathogens. The activation of phagocyte NADPH oxidase requires membrane translocation and the binding of several cytosolic factors, including p47, p67, and Rac1. Our cryo-EM studies reveal that the p67-Rac1 complex clamps on the dehydrogenase domain (DH) of NOX2 and induces its contraction, stabilizing the binding of NADPH and resulting in a reduction of the distance between the NADPH-binding domain (NBD) and the FAD-binding domain (FBD). Additionally, DH docks onto the bottom of the transmembrane domain (TMD) of NOX2, leading to a shortened distance between the FAD and the inner haem. These structural rearrangements might facilitate the efficient electron transfer between the redox centers within NOX2, leading to the activation of phagocyte NADPH oxidase.

Key words: NOX, NOX2, NADPH, superoxide, ROS

Short CV

Lei Chen received his Ph.D. from Tsinghua University. He was working on the mechanism of AMPK. After that, he moved to Oregon Health and Science University as a postdoctoral researcher in the lab of Eric Gouaux, studying the mechanism of AMPA receptors. He started his own lab in Peking University in 2016. His lab focuses on the molecular mechanism of proteins involved in human diseases, especially metabolic diseases and cardiovascular diseases.

OGG1 promotes iTreg differentiation and alleviates mouse IBD by facilitating Foxp3 transcriptional activation

Xueqing Ba (巴雪青)

School of Life Sciences, Northeast Normal University, China

Email: baxq755@nenu.edu.cn

Abstract

8-Hydroxyguanine (8-oxoGua) is one of the most prevalent forms of oxidative damage of DNA bases due to guanine's low redox potential. The 8-hydroxyguanine DNA glycosylase 1 (OGG1) is a cognate DNA repair enzyme that specifically recognizes 8-oxoGua and initiates base excision repair pathway to ensure genomic fidelity. However, guanine oxidation has an evolutionary bias within the genome and tends to occur in transcriptional regulatory regions. Thus, 8-oxoGua is beyond a lesion requiring repair, but may be an epigenetic-like modification in response to oxidative stress. Correspondingly, OGG 1 can serve as a specific "reader" of this base modification, playing function in transcriptional regulation of inflammatory genes independent of its repair activity.

Our present study further revealed that OGG1 deficiency reduces iTreg differentiation and aggravates mouse IBD colitis. Mechanically, the enzymatically inactive OGG1 binds to the promoter and CNS1 of Foxp3, promoting the recruitment of Smad3 to enhance Foxp3 transcription. Additionally, at the epigenetic level, binding of OGG1 to 8-oxoGua results in the demethylation of Foxp3 promoter and CNS2 via recruiting Tet1/2 and expelling Dnmt1, which in turn activates Foxp3 transcription. Furthermore, the OGG1S326C mutant, which has been taken as a susceptibility factor for many diseases such as lung diseases, with frequency up to ~20% in the human population, exhibits a stronger effect on iTreg differentiation induction than its wild-type counterpart, thus is negatively correlated with the incidence of IBD. Finally, OGG1 inhibitor O8, which inhibits imine formation in OGG1 without blocking its substrate binding, was able to promote mouse and human iTreg differentiation, and then effectively alleviate IBD in mice.

This work not only expands our understanding of the mechanism by which OGG1 promotes gene transcriptional activation and the dual roles of OGG1 in inflammation modulation, but also provides new targets for intervention in autoimmune diseases such as IBD.

Key words: oxidative stress, inflammation, OGG1, transcription regulation

Short CV

Xueqing Ba, Ph.D

Professor, the School of Life Science, Northeast Normal University. Research interest has long been focusing on the oxidative stress response of cells, especially the effect of DNA oxidation in chromatin-based biological processes. Among bio-marcromolecules, DNA is vulnerable to ROS due to the low redox potential of the nucleobases, and out of them, guanine is the most susceptible to being oxidized. The resultant base lesion 8-oxo-7, 8-dihydroguanine (8-oxoGua) is commonly regarded as a biomarker of oxidative stress and is repaired through 8-oxoguanine DNA glycosylase 1 (OGG1)-initiated base excision repair (BER) pathway. Our recent studies, together with the research by laboratories including Dr. Boldogh', Dr. Lloyd', Dr. Mitra', Dr. Burrow' and others', revealed the epigenetic role of 8-oxoGua and the "reader" function of OGG1 leading to gene expression during inflammation and tumorigenesis. This is supported by our original research (Li et al. BBA-Dis, 2024; Zheng et al., Redox Biol, 2023; Pan et al., Nucleic Acids Res, 2023; Hao et al, FASEB J, 2020; Hao et al. Redox Biol, 2018; Ba and Boldogh, Redox Biol (review), 2018; Wang et al, Cell Mol Life Sci, 2018; Wang et al, Cell Death & Dis, 2018; Pan et al. J Biol Chem, 2016).

A lactate-lipid peroxidation-acetate metabolic axis between tumor-associated macrophages and cancer cells fuels hepatocellular carcinoma metastasis

Ming Lu (鲁明)

Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences, China

Email: mlu@sinh.ac.cn

Abstract

High abundance of acetyl-CoA is a critical metabolic feature in metastatic cancers. To sustain high level of acetyl-CoA, cancer cells actively uptake acetate for acetyl-CoA biosynthesis in various cancer types. However, the source of acetate in the cancer microenvironment remains largely undetermined. Here, using hepatocellular carcinoma (HCC) models, we demonstrate that tumor-associated macrophages (TAMs) promote acetate accumulation in HCC cells by secreting acetate to cancer microenvironment. Mechanistically, lipid peroxidation-ALDH2 pathway is responsible for the acetate production in TAMs. Inhibition of ALDH2 in TAMs suppresses the pro-migration effect of TAMs on HCC cells in vitro. In orthotopic HCC mice model, genetic ablation of ALDH2 in TAMs reduces acetate levels in primary HCC cells, and significantly diminishes HCC lung metastasis *in vivo*. Finally, we identify HCC cells-derived lactate as the upstream inducer of lipid peroxidation-ALDH2 pathway in TAMs. Collectively, our findings reveal a lactate-lipid peroxidation-acetate metabolic cross-talk between HCC cells and TAMs, which positions TAMs as an acetate reservoir to fuel HCC metastasis.

Key words: Tumor-associated macrophages, Lipid peroxidation, Acetate, HCC metastasis, Lactate

Short CV

Ming Lu, Principal Investigator in Shanghai Institute of Nutrition and Health (SINH), Chinese Academy of Sciences (CAS).

Brief Biography:

Ph.D./Postdoc Institute of Biochemistry and Cell Biology, CAS; Assistant/associated research fellow, Huashan Hospital, Fudan University; Visiting scientist, The Jackson Laboratory, US; Principal Investigator, SINH, CAS.

Research interests:

Our lab focuses on the roles of lipid metabolic aberrations in cancer metastasis and microenvironmental redox status.

Selected Publications:

Corresponding Author: Cell Metabolism 2019, 29(4): 886-900; Cancer Letters 2024, 592: 216903; Cell Rep, 2022, 39(3):110712.

First/co-first Author: Cancer Cell 2016, 30(3): 444-458. Nature Immunology 2020, 21(11): 1444-1455; Nature Communications 2020, 11(1): 4387.

STING: a potential target for suppressing the development of clonal hematopoiesis and leukemia

Yuheng Shi (石玉衡)

Institutes of Biomedical Sciences, Fudan university, China

Email: shiyuheng@fudan.edu.cn

Abstract

Clonal hematopoiesis (CH) is a significant risk factor for numerous diseases, including hematopoietic malignancies, atherosclerosis, ischemic stroke, gout, and chronic liver injury. Mutations in DNMT3A and TET2, which occur in approximately 70% of CH patients, are considered as initial triggers for leukemia. Despite this, effective strategies to prevent the progression of CH to leukemia are lacking. Our study demonstrates that targeting STING effectively prevents the development of CH harboring these mutations. Mechanistically, the loss of TET2 or DNMT3A activates the STING pathway, leading to chronic inflammation in DNA-modifying enzyme-deficient hematopoietic progenitor/stem cells. This inflammatory response in the bone marrow promotes increased self-renewal and skewed lineage differentiation of mutated HSPCs. Moreover, targeting STING activates FADS2 in AML1-ETO fusion leukemia cells, causing lipid-peroxidation-associated cell death. Collectively, our findings highlight STING as a potent target for preventing hematological diseases.

Key words: Clonal hematopoiesis, DNA modification, STING, Lipid peroxidation

Short CV

Dr. Yuheng Shi is an associate professor at the Institutes of Biomedical Sciences, Fudan University. His research primarily focuses on the role of inflammation in tumor initiation, the epigenetic regulation of leukemia development, and the identification of therapeutic targets. Dr. Shi has made series of progresses in understanding the mechanisms behind hematopoietic diseases related to mutations in DNA-modifying enzymes. His work has been published in journals such as Leukemia, Nature Communications, and Cell Reports.

Disorder of nitration/S-sulfhydration participates in hyperhomocysteinemia progression and liver damage

Wen Wang (王雯)

Department of Pathology and Pathophysiology, School of Basic Medical Sciences, Capital Medical University, Beijing, China

Email: wangwen@ccmu.edu.cn

Abstract

In recent years, studies have found that hyperhomocysteinemia (HHcy) has become an important risk factor for liver diseases. Meanwhile, homocysteine was mainly metabolized in liver. It is of great significance to clear out the relationship between HHcy and liver damage and reveal the underlying mechanism. Our study has found that HHcy increased the level of nitration of CBS and CSE, resulting in the inhibition of their activity. HHcy also decreased the expression level of CSE. *In vivo*, Hcy is negatively correlated with hydrogen sulfide (H2S) levels. HHcy decreased the S-sulfhydration level and activity of the Sp1-CSE-H2S pathway. The rise of nitration in HHcy led to insufficient S-sulfhydration. The decrease in H2S level inhibited MTHFR S-sulfhydration and its activity. This study proposed a vicious cycle of H2S signaling in Hcy metabolism, and emphasized the potential role of H2S in the treatment of HHcy. Furthermore, we found that HHcy promoted nitration of nuclear receptor coactivator 4 (NCOA4), up-regulate the level of ferritinophagy, cause a significant increase in intracellular free iron content, and increase the susceptibility to ferroptosis, thereby promoting the occurrence and development of liver injury. Our study also concluded that NaHS supplementation mitigates HHcy-induced liver injury by downregulating hepatic autophagy through the S-sulfhydration and activation of glucocorticoid-regulated kinase 1 (SGK1). In conclusion, the disorder of nitration/S-sulfhydration participates in HHcy progression and liver damage. The potential therapeutic application of H2S and anti-nitration in treating liver damage associated with HHcy presents a new avenue for research and clinical application.

Short CV

Professor, Doctoral Supervisor, Deputy Director of the Department of Physiology and Pathophysiology, School of Basic Medical Sciences, Capital Medical University, and Deputy Director of the Beijing Key Laboratory for Metabolic Disorder-Related Cardiovascular Diseases. Her research interest mainly focuses on abnormal oxidation-reduction modification and homocysteine metabolic disorder, whose work have been published in Cardiovasc Res, Antioxid Redox Signal and Free Radic Biol Med, et al as corresponding authors.

Endothelium-dependent contraction, NO and cardiovascular disorders in the absence of prostacyclin synthesis

Bin Liu (刘斌)

Shantou University Medical College, China

Email: bliu@stu.edu.cn

Abstract

Prostaglandin I2 (PGI2) synthesized by endothelial cyclooxygenase (COX) evokes potent vasodilation in some blood vessels but is paradoxically responsible for endothelium-dependent constriction (EDC) in others. However, how PGI2 synthase (PGIS) deficiency affects EDC and how this is implicated in the consequent cardiovascular pathologies remain largely unknown. Experiments were performed on WT, Pgis knockout (Pgis-/-) and Pgis/thromboxane-prostanoid receptor gene (Tp) double knockout (Pgis-/-Tp-/-) and Pgis-/- mice transplanted with unfractionated WT or Cox-1-/- bone marrow cells, as well as human umbilical arteries. PGF2α, PGE2 and a trace amount of PGD2, but not thromboxane A2 (TxA2), were produced in response to acetylcholine (ACh) in Pgis-/- or PGIS-inhibited arteries. PGIS deficiency resulted in augmentation of EDC ex vivo and *in vivo*. Endothelium-dependent hyperpolarization was unchanged, but phosphorylation levels of endothelial nitric oxide synthase (eNOS) at Ser1177 and Thr495 were altered and NO production and the NO-dependent relaxation evoked by ACh were remarkably reduced in Pgis-/- aortas. Blood pressure and the cardiac parameters remained normal in Pgis-/- mice at 8-10 weeks, but later the mice sequentially developed high blood pressure, vascular remodeling and cardiac hypertrophy. Additional ablation of TP not only restrained EDC and the downregulation of NO signaling in Pgis-/- mice, but also ameliorated the cardiovascular abnormalities. Stimulation of Pgis-/- vessels in the presence of platelets led to increased TxA2 generation. COX-1 disruption in bone marrow-derived cells failed to affect the development of high blood pressure and vascular remodeling in Pgis-/- mice though it largely suppressed the increase of plasma TxB2 (TxA2 metabolite) level. The non-TxA2 prostanoids/TP axis plays an essential role in mediating the augmentation of EDC, the decrease of NO and the cardiovascular disorders when PGIS is deficient, suggesting TP as a promising therapeutic target in diseases associated with PGIS insufficiency.

Key words: prostacyclin, hypertension, endothelial dysfunction, endothelium

Short CV

Dr. Bin Liu is a professor at Shantou University Medical College. He received his PhD degree from Institute of Chemistry, Chinese Academy of Sciences and completed his postdoctoral training at the Ohio State University. His research interests involve COX products, NO and ROS in heath and diseases and his recent work has been published in journals such as Circ Res and Kidney Int.

SIRT2 governs a cytoplasm-mitochondrial signal to repress mitochondrial ROS and vascular ageing

Hou-Zao Chen (陈厚早)

Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences & Peking Union Medical College, 5 Dong Dan San Tiao, Beijing 100005, China

Email: chenhouzao@ibms.cams.cn

Abstract

Cardiovascular diseases are the leading causes of death and disability in the world. A better understanding for the molecular mechanism in the development of cardiovascular diseases will provide more strategies for their diagnosis, treatment and prevention. Mammalian SIRTuins regulate metabolism and aging-related diseases, including diabetes and cardiovascular diseases. Among the SIRTuins, the cytosol member histone deacetylase SIRT2 is less characterized. Our group had previously shown that SIRT2 in the heart represses aging-related cardiac hypertrophy, at least in part, by maintaining signaling through the liver kinase B1 (LKB1)-AMPK pathway, the central pathway controlling various aspects of metabolism. Sirt2-KO promoted aging-related cardiac hypertrophy and caused cardiac dysfunction. However, Sirt2-KO attenuated metformin-induced activation of AMPK signaling and, subsequently, the cardioprotective functions of metformin in hypertrophic hearts. The results of recent studies from our lab showed that SIRT2 expression was highest in mouse aortas among the SIRTuin family and decreased in vascular smooth muscle cells (VSMCs) of aged aortas. Sirt2-KO promoted vascular remodeling in aged aortas. SIRT2 governs a cytoplasm-mitochondrial signal to repress mitochondrial ROS and vascular ageing. SIRT2 plays a protective role in age-related vascular dysfunction. Therefore, SIRT2 activation may represent a promising strategy for managing age-related cardiovascular dysfunction.

Short CV

Dr. Hou-Zao Chen is currently a professor of State Key Laboratory of Common Mechanism Research for Major Diseases, Department of Biochemistry and Molecular Biology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (CAMS) & Peking Union Medical College (PUMC). Dr. Chen's research expertise is molecular mechanisms of age-related cardiovascular diseases, particularly the role of epigenetic regulation in the development and progression of atherosclerosis, diabetic vascular disease, aortic aneurysm and cardiac hypertrophy. He has published more than 60 original research articles and invited reviews including Sci Immunol.2024; Nat Commun.2024,2022; Cell Rep.2024; Euro Heart J.2023,2017; Proc Natl Acad Sci U S A.2022; Circ.2021,2016; Nat Cell Biol.2019; J Exp Med.2016; Circ Res.2016,2011; Cell Syst.2015; Aging Cell 2014, which have been cited more than 5000 times. Throughout his academic career, Dr. Chen has received numerous awards including National Funds for Distinguished Young Scientists in China. He has served as Editorial Board Member for Free Radical Biology and Medicine and Cardiovascular Drugs and Therapy.

Tetrahydrobiopterin is a promising target of diabetic cardiomyopathy via restoring mitochondria function

Hyoung Kyu Kim

Inje University, Korea

Email: estrus74@gmail.com

Abstract

Diabetic cardiomyopathy (DCM) is a major cause of mortality/morbidity in diabetes mellitus patients. Although tetrahydrobiopterin (BH4) shows therapeutic potential as an endogenous cardiovascular target, its effect on myocardial cells and mitochondria in DCM and the underlying mechanisms remain unknown. Here, we determined the involvement of BH4 deficiency in DCM and the therapeutic potential of BH4 supplementation in a rodent DCM model. We observed a decreased BH4:total biopterin ratio in heart and mitochondria accompanied by cardiac remodeling, lower cardiac contractility, and mitochondrial dysfunction. BH4 supplementation improved cardiac function, corrected morphological abnormalities in cardiac muscle, and increased mitochondrial activity. In the diabetic heart, a decrease in PGC1a, which is important for regulating mitochondrial biosynthesis, was confirmed, and BH4 significantly increased its level. Mechanistically, BH4 bound to calcium/calmodulin-dependent protein kinase kinase 2 (CaMKK2) and activated downstream AMP-activated protein kinase/cAMP response element binding protein/PGC-1α signaling to rescue mitochondrial and cardiac dysfunction in DCM. These results suggest BH4 as a novel endogenous activator of CaMKK2.

Key words: Tetrahydrobiopterin, mitochondria, diabetic cardiomyopathy

Symposium-YIO-2 (Y-2)

Redox and cancer, infection and immunity
Redox and environmental challenge

Chair: Jianghong Man (满江红)

National Center of Biomedical Analysis, Beijing, China

Email: jhman@ncba.ac.cn

Short CV

The current focus of Dr. Man's research program is to identify specific protein targets and key regulators that control the maintenance of cancer stem cells (CSCs) in glioblastoma progression. The major purpose of his research is clarifying how CSC maintain its stemness and associate with the microenvironments to promote tumor growth, contribute therapeutic resistance and recurrence.

Education

2015 − now, Professor, National Center of Biomedical Analysis (NCBA), Beijing, China

2012 − 2015, Postdoctoral Fellow, Cleveland Clinic, Cleveland, OH, USA

2002-2008, Ph.D., National Center of Biomedical Analysis (NCBA), Beijing, China

1994-1999, M.D., China Medical University, Shenyang, China

Peer-reviewed Publications

1. Dake Xiao, Haowen Ran, Lishu Chen, ..., Jianghong Man*. FSD1 inhibits glioblastoma diffuse infiltration through restriction of HDAC6-mediated microtubule deacetylation. SCIENCE CHINA Life Sciences. 2024, (accepted)

2. Lishu Chen, Qinghui Qi, Xiaoqing Jiang, Jin Wu, ..., Jianghong Man*. Phosphocreatine promotes epigenetic reprogramming to facilitate glioblastoma growth through stabilizing BRD2. Cancer Discovery. 2024, Aug 2;14(8):1547-1565.

3. Chen L, Zhou C, Chen Q, ..., Man J*. Oncolytic Zika virus promotes intratumoral T cell infiltration and improves immunotherapy efficacy in glioblastoma. Mol Ther, 2022 Feb 1;24:522-534.

4. Haohao Huang, Songyang Zhang, Yuanyuan Li, ..., Jianghong Man*. Suppression of mitochondrial ROS by prohibitin drives glioblastoma progression and therapeutic resistance. Nature Communications, 2021, Jun 17;12(1):3720.

5. Xiaoyan Zhan, Saisai Guo, ..., Jianghong Man*. Glioma stem-like cells evade interferon suppression through MBD3/NuRD complex-mediated STAT1 downregulation. The Journal of Experimental Medicine, 2020 May 4;217(5).

Chair: Chung S. Yang

Rutgers, The State University of New Jersey, USA

Email: csyang@emeritus.rutgers.edu

Short CV

Dr. Chung S. Yang is a Distinguished Professor Emeritus at Rutgers University, New Jersey, USA. He is noted for his research on disease prevention by dietary constituents such as tea, vitamin E, and other agents. His research group studied the fundamental mechanisms of cancer formation and prevention in animal models and extended the research to humans. Dr. Yang is one of the first group of scientists to conduct collaborative research in China in 1979 after US and China established normal diplomatic relationship and, soon afterwards, he helped to establish the large scale Linxian Nutritional Intervention Trial (LNIT). This unique US - China collaborative study found that supplementation with a combination of vitamin E, beta-carotene, and selenium for 63 months decreased mortality due to gastroesophageal cancer. His collaborative research and teaching in China have continued for 45 years today.

Dr. Yang has trained over 100 research students/associates and has authored more than 600 publications. He was elected Fellow of the American Association for the Advancement of Science in 2010 and received the First Lu Yu Award from the China Tea Science Society in 2021.

Two sesquiterpene lactones inhibit TXNRD1 and induce endoplasmic reticulum stress in cancer cells

Jianqiang Xu (许建强)

Dalian University of Technology, China

Email: jianqiang.xu@dlut.edu.cn

Abstract

Inhibiting selenoprotein TXNRD1 with lead compounds or effective drugs is beneficial for enhancing chemotherapy in clinicals. In this study, we identified two sesquiterpene lactone compounds, ergolide (Ergo) and eupalinolide K (EupK), are effective inhibitors of TXNRD1. TXNRD1 mutants' activity assay and LC-MS/MS analysis revealed that Ergo and EupK targeted the Sec498 residue of TXNRD1 through the Michael addition. The inhibition of TXNRD1 by Ergo and EupK, abolished the disulfide reductase activity but increase superoxide production via the inherent NADPH oxidase activity of the enzyme. In cellular condition, the cytotoxicity of Ergo and EupK is associated with oxidative stress and endoplasmic reticulum (ER) stress, and ultimately leading cancer cells to apoptosis in HCT116 cells. Meanwhile, we demonstrated that TXNRD1 inhibition may up-regulate NRF2, and Ergo's cytotoxicity was slightly increased when NRF2 activation was suppressed. Furthermore, we compared Ergo and EupK with another four sesquiterpene lactone compounds when incubating with TXNRD1, using LC-MS/MS analysis. Our results showed that the Cys64 residue is an effective binding site for the TXNRD inhibitor parthenolide (Part), and a notable preclinical TXNRD1 inhibitor TRi-1 can bind to Cys59 residue, indicating that N-terminal redox motif is also a target site for TXNRD1 inhibitors besides the redox active C-terminal motif. Taken all, this study may improve our understanding of TXNRD1 binding and inhibition, and provided new insights into the development of effective small molecules targeting TXNRD1.

Key words: thioredoxin reductase, sesquiterpene lactone, SecTRAPs, disulfide stress, ER stress, NRF2

Short CV

Xu is an associate professor in School of Chemical Engineering, Ocean Technology & Life Science @ Dalian University of Technology (DUT). He completed his B.S.(200207)/Ph.D.(200810) with Prof. Qing Yang in Dalian, and got his PostDoc training (200902-201409) with Prof. Elias Arner @ Karolinska Institutet in Stockholm. Since 201512, he was leading a research lab on selenobiology at Panjin Campus of DUT. His lab focuses on TXNRD1/2 & GPX1/4 regulating emerging PCDs & tumor cell drug resistance. He has published >50 peer reviewed research papers and the current H-index is 27.

Novel anticancer drug discovery strategies by targeting NQO1

Xiuping Chen (陈修平)

University of Macau, Taipa, Macao, China

Email: xpchen@um.edu.mo

Abstract

NAD(P)H: quinone oxidoreductase 1 (NQO1) is an enzyme expressed in high levels in multiple solid tumors, making it an appealing prospect as an anticancer drug target, specifically in regard to NQO1 positive (NQO1+) tumors. β-lapachone (β-lap) is a drug targeting NQO1 that is presently undergoing clinical trials. β-lap selectively kills NQO1+ cancer cells by instigating reactive oxygen species (ROS) through catalytic activation of NQO1. Here, we found that cryptotanshinone (CTS), a natural compound, triggers NQO1-dependent necrosis without impacting NQO1 activity. The impact of CTS on NQO1 was measured using cellular thermal shift assay, enzymatic activity assay, and tryptophan fluorescence titration. The interaction between CTS and NQO1 was examined using molecular docking. The downstream signalings of NQO1, including iron, Ca2+, c-Jun N-terminal kinase 1/2 (JNK1/2), and poly(ADP-ribose) polymerase (PARP) in response to CTS were investigated using inhibitors, siRNA, and other methods. The results showed that CTS selectively kills NQO1+ cancer cells by inducing NQO1-dependent non-apoptotic necrosis. It is interesting to note that CTS directly binds to NQO1 but does not activate its catalytic activity. Moreover, CTS selectively suppressed the growth of the tumor in the NQO1+ xenograft model, which was reversed by the NQO1 inhibitor and NQO1 shRNA. In addition, the combination of CTS with β-lap shows a significant synergistic anticancer effect. This study demonstrates the non-enzymatic function of NQO1 in triggering cell death, offering new avenues for the creation of NQO1-targeted drugs against cancer.

Key words: NQO1, ROS, Cancer, Drug discovery

Short CV

Dr. Xiuping Chen obtained his Ph. D degree from Peking Union Medical College in 2007. Since Aug 2010, he worked as an assistant professor at University of Macau and was promoted to associate and full professor in 2015 and 2021, respectively. Dr. Chen's research focuses on pharmacology. He aims to screen and identify regulators of programmed cell death (PCD) and epithelial-mesenchymal transition (EMT) from natural compounds as leads or potential drugs for the treatment of cancer, cardiovascular diseases, and fibrotic diseases. He is the winner of The 17th SERVIER Young Pharmacologist Award in 2013 and the winner of Second prize of the Macao Science and Technology Awards in 2012 and 2014. Dr. Chen is a Member of the Royal Society of Biology since 2023. Dr. Chen has > 150 publications with >14,000 citations. The h-index is 63.

Structure-activity relationship and biomedical applications of nanozymes

Kelong Fan (范克龙)

Institute of Biophysics, Chinese Academy of Sciences, China

Email: fankelong@ibp.ac.cn

Abstract

Nanozymes, a novel class of nanomaterials exhibiting enzymatic properties, have gained significant attention in the biomedical field due to their multifunctionality, tunable catalytic activity, and exceptional stability. Despite these advantages, nanozymes still fall short in catalytic efficiency and diversity when compared to natural enzymes. This talk delves into the structure and function of nanozymes, with a focus on the active sites and catalytic microenvironments of natural enzymes as a blueprint. Through de novo design and biomimetic synthesis, we achieved rational design and activity optimization of iron-based and single-atom nanozymes, proposing a comprehensive structure-activity relationship for these materials. Leveraging this relationship, we pioneered new applications of nanozymes in tumor catalytic therapy, prodrug activation, and the construction of nanozyme organelles. These advancements pave the way for innovative approaches in the diagnosis and treatment of major diseases, offering fresh perspectives and technologies for the medical field.

Key words: Nanozymes, Structure-Activity Relationship, Biomedical Applications

Short CV

Kelong Fan received his Ph.D. degree in cell biology from the Institute of Biophysics, Chinese Academy of Sciences, in 2014. After this period, he stayed there to further pursue 3 years of postdoc training and 2 years of associate professor work experience before attaining a full professor position in 2019. He is interested in exploring the novel functions and applications of nanozymes in biomedicine, with a top priority to design functional nanozymes by learning from nature, and to develop novel strategies for disease theranostics. He is recognized as "Highly Cited Researcher" by Clarivate in 2022-2023 and now serves as Deputy Editor of Exploration.

Electron FLASH irradiation ameliorates radiation-induced developmental and neurological toxicity in zebrafish model

Cuixia Di (狄翠霞)

Institute of Modern Physics, Chinese Academy of Sciences, China

Email: dicx@impcas.ac.cn

Abstract

Ultra-high dose rate irradiation, also named Flash radiotherapy, emerged as a new milestone in the field of cancer radiotherapy, which has been shown to spare normal tissues while preserving the therapeutic effect on tumors compared to conventional irradiation (Conv). However, successful clinical translation of Flash radiotherapy depends on a better understanding of the underlying biological mechanisms. In this study, we leveraged the zebrafish model in radiobiological research to explore the amelioration of radiation-induced neurodevelopmental toxicity. The findings of this study demonstrated that electron Flash radiotherapy can reduce radiation-induced developmental and neurological toxicity and may provide long-term benefits, suggesting the potential utilization of this modality for the clinical management of patients requiring cranial radiation therapy.

Key words: Flash radiotherapy, Zebrafish model, Neurobehavior, Developmental neurotoxicity, Neuroinflammation

Short CV

Di Cuixia, Ph. D., researcher, professor, specializes in the mechanism of heavy ion therapy. Her work is to reveal the molecular mechanism of Alternative splicing in overcoming the radiosensitivity of cancer cells to heavy ions. Published more than 60 articles in well-known international journals such as Cell Death and Differentiation, J Exp Clin Cancer Res. Participated in Program 973 projects and key R & D projects of the Ministry of Science and Technology. Now responsible for the key R & D projects of the Ministry of Science and Technology. She has won provincial and ministerial awards for science and technology many times.

Supersulfide regulation of innate immune responses

Tomohiro Sawa

Graduate School of Medical Sciences, Kumamoto University, Japan

Email: sawat@kumamoto-u.ac.jp

Abstract

Cysteine is an amino acid having thiol as a functional group, and plays an essential role in maintaining the structure of proteins through disulfide bonds. It also acts as an antioxidant, and enzyme activity center within cells. In recent years, cysteine persulfide and polysulfides, in which sulfur atoms are conjugated (sulfur catenation) to the cysteine thiol group, are abundantly present in cells as forms of glutathione and protein persulfides and polysulfides, and they have a wide variety of biological effects such as extremely strong antioxidant activity, anti-inflammatory effects, regulation of immune function, and control of energy metabolism. These diverse biological functions are not found in the original cysteine thiols, or are much stronger, so it is called supersulfides, meaning that it has functions that exceed those of sulfides. Currently, the metabolism and functional regulation of supersulfides are attracting a great deal of attention worldwide as targets for new drug discovery and diagnosis. We are currently investigating the roles of supersulifdes on innate immune responses. In this study, regulatory roles of supersulfides on neutrophil functions, particularly focusing on the effects of supersulfides on neutrophil mediated bacterial killing and host defense.

Key words: Innate immunity, neutrophil, supersulfides, bacterial infection, glutathione

Supersulfides regulate NLRP3 inflammasome activation through sensing homeostasis

Tianli Zhang

Center for Integrated Control, Epidemiology and Molecular Pathophysiology of Infectious Diseases, Akita University, Japan

Email: zhangtianli220@hotmail.com

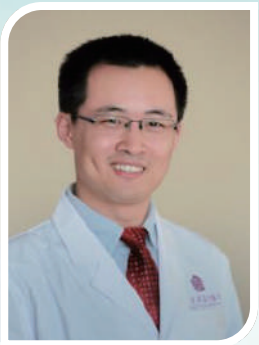
Abstract

The activation of the nucleotide-binding domain, leucine-rich repeat domain and pyrin domain-containing protein 3 (NLRP3) inflammasome is precisely regulated to prevent excessive innate immune and inflammatory responses. Despite numerous proposed mechanisms for regulating NLRP3 inflammasome activation, the checkpoints governing this process remain elusive. Here, we demonstrate that supersulfidation, a reversible post-translational modification of protein cysteine residues to persulfides or polysulfides, occurs endogenously to modulate NLRP3. This modification plays a crucial role in the NLRP3 inflammasome activation throughout whole processes, including priming, assembly and activation. Furthermore, supersulfidation of NLRP3 is implicated in homeostasis-altering molecular processes, such as potassium efflux and redox imbalance within macrophages. More importantly, enhancing supersulfides using a chemical donor significantly halts NLRP3 inflammasome activation both in vitro and *in vivo* by regulating NLRP3 supersulfidation. Our findings provide new insights into the endogenous mechanisms of NLRP3 inflammasome activation and constitute a potential therapeutic strategy for NLRP3 inflammasome-associated inflammatory diseases.

Key words: Reactive Sulfur Species, Supersulfides, NLRP3 inflammasome, Immune Responses, Inflammatory Responses

Short CV

I am an assistant professor at Akita University, Japan.Myresearch focuses on the regulatory mechanisms ofimmune and inflammatory responses from theperspective of supersulfides. I have developed supersulfide donors and demonstrated that supersulfides regulate immune responses by counteracting Toll-like receptor signaling. I also discovered that intracellular glutathione and its persulfides efflux are necessary for NLRP3 inflammasome activation.



OSA induced multiple-system damage via oxidative stress

Guoping Yin (尹国平)

Beijing Tsinghua Changgung Hospital, Beijing, China

Email: yinguoping311@163.com

Abstract

Obstructive sleep apnea (OSA), affecting approximately 1 billion adults globally, is characterized by recurrent airway obstruction during sleep, leading to oxygen desaturation, elevated carbon dioxide levels, and disrupted sleep architecture. OSA-related complications include cardiovascular disorders, neurological impairments, metabolic dysfunction, and a potential link to cancer. OSA significantly impacts quality of life and is associated with increased morbidity and mortality, particularly in the cardiovascular and cognitive domains. The cyclic pattern of intermittent hypoxia in OSA triggers oxidative stress, contributing to the multiple-system damage. Understanding the role of oxidative stress in OSA will help to clarify the etiology and discover new treatment options, which will be of great signifcance for better clinical intervention.

Key words: Obstructive sleep apnea, Oxidative stress, Intermittent hypoxia, Multiple-system damage

Short CV

Guoping Yin, tenured associated professor of Tsinghua university.Member of the Sleep Medicine Professional Committee of the Chinese Medical Association, standing committee member and deputy secretary-general of Sleep Medicine Committee of the China International Healthcare Promotion Association, member of Otolaryngology Head and Neck Surgery Committee of Chinese Medical Association. Focus on the basic and clinical research of sleep disorder breathing. Up to now, has sponsored one general project of National Natural Science Foundation of China, as the key member participated 6 general project of National Natural Science Foundation of China and 1 National Key R&D Project of Science and Technology Ministry of China. As first or corresponding author published 13 high- level papers in this area, as co-author published 43 papers.

HTHB: A Potential Therapeutic Agent for Cognitive Impairment and Inflammation

Jiangang Long (龙建纲)

Xi'an Jiao Tong University, China

Email: jglong@mail.xjtu.edu.cn

Abstract

Improving the function of central nervous system and peripheral metabolic organs simultaneously is an effective strategy to delay aging. 2-(3,4-Dihydroxyphenyl)ethyl 3-hydroxybutanoate (HTHB), a novel derivative of hydroxytyrosol (HT) synthesized by our laboratory, has shown promising metabolic and anti-inflammatory properties. We explored the mechanism of HTHB in improving brain function. In sleep deprivation (SD) rats, HTHB treatment significantly ameliorated behavioral disorders, reduced brain oxidative stress, and alleviated mitochondrial DNA (mtDNA) oxidation and release. This reduction in mtDNA oxidation and efflux was associated with decreased activation of pro-inflammatory cytokines and NF-κB. Research on senescence-accelerated mouse prone 8 (SAMP8) mice demonstrated that HTHB effectively mitigates memory decline, reduces inflammation in the brain cortex, intestine, and peripheral system, and modulates gut microbiota dysbiosis. Behavioral testing, biochemical detection, and 16S RNA analysis revealed that HTHB treatment enhances gut barrier integrity and rescues tight junction protein levels impaired by lipopolysaccharide (LPS) in vitro.

Together, these studies underscore the therapeutic potential of HTHB in addressing cognitive impairment and inflammation. The research on HTHB provides new experimental evidence for addressing disease- or aging-induced cognitive decline.

Key words: HTHB; Cognitive function; mitochondrial DNA; Gut microbiota; Inflammation

Short CV

- 2006-2009: Postdoctoral Researcher, University of California, Irvine and Sunhealth (Banner Health) Research Institute, USA
- 2009-2011: Associate Professor, School of Life Science and Technology, Xi'an Jiaotong University
- 2011-Present: Professor (Young Key Teacher) and Ph.D. Supervisor, School of Life Science and Technology, Xi'an Jiaotong University
- 2015-2016: Deputy Dean, School of Life Science and Technology, Xi'an Jiaotong University
- 2016-Present: Deputy Dean, Graduate School, Xi'an Jiaotong University

Symposium-YIO-3 (Y-3)

Redox and neural function and mental health

Chair: Wen li Li (李文丽)

The Fourth Military Medical University, China

Email: liwenli@fmmu.edu.cn

Short CV

Wenli Li, Professor of Department of Toxicology, Expert for the International Organization for the Prohibition of Chemical Weapons. Prof. Li received her Master Degree in Preventive Medicine in 1996 and PhD in 2004 from The Fourth Military Medical University. She studied in the University of Tokyo in Japan for one year as visiting professor. Prof. Li cooperated research on phosgene with Inhalation Toxicology Laboratory of Bayer in Germany for ten years. She has been focusing on the study of the molecular mechanism and prevention of injury caused by industrial poisons, especially on lung injury induced by phosgene. She also focused on the studies of antioxidants in free radical biology and medicine. Prof. Li has received 4 projects of the National Natural Science Foundation, 2 international cooperation projects, 1 Key research and development project of Shaanxi Province and so on. She published more than 50 scientific papers in peer-reviewed journals and participated two books in the world, named Inhalation Toxicology and Chemical Warfare Agent as editor. She is on the editorial board of Inhalation Toxicology, the vice chairman of the Shaanxi Toxicology Society, the member of the International Phosgene Safety Group, a Committee Member of the Free Radical Biology and Medicine Branch of the Chinese Biophysical Society.

Chair: Changyang Gong (巩长旸)

Sichuan University, China

Email: chygong14@163.com

Short CV

Prof. Changyang Gong received his Ph.D. degree in cell biology from Sichuan University, Chengdu, China, in 2010. He is currently a Professor of pharmaceutics at State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, China. His current research focuses on novel drug and gene delivery system for tumor therapy, nanomedicine, and immune adjuvant for tumor vaccine. He has published three book chapters and more than 120 peer-review scientific papers in Nat Commun, J Am Chem Soc, Adv Mater, Adv Funct Mater, Adv Sci, ACS Nano, Adv Drug Deliver Rev, Biomaterials, J Control Release etc. He is Editorial Board of Chinses Chemical Letters and BioMed Research International. His scientific achievements have been honored by the National Natural Science Foundation for Excellent Young Scholars (2018) and the National Program for Support of Top-notch Young Professionals of China (2015).

Redox biomarkers for prognosis of infectious diseases

Jun Wang (王军)

Hubei University of Technology, China

Email: jun_wang@hbut.edu.cn

Abstract

Oxidative stress is essentially caused by an imbalance between oxidizing reagents and reducing reagents in body. In viral infections, oxidative stress has been reported arising. However, whether oxidative stress still exists during recovery or under treatment is barely investigated. In one cohort study for patients recovered from COVID-19 or with long-COVID, blood and urine nitrate levels were found significantly higher than those who never got infected. In another cohort study for HIV-infected patients or patients with AIDS-related lymphoma (ARL), nitrate, malondialdehyde, total antioxidant capacity differentiated ARL and HIV-only patients. In addition, levels of nitrite, 3-nitrotyrosine, malondialdehyde and total antioxidant capacity were different between ARL patients who were still alive and those who passed away within one year after blood collection. In short, redox markers may provide useful insights for prognosis of virus-triggered diseases.

Key words: redox biomarker, prognosis, infectious disease, long-COVID, HIV

Short CV

Dr. Jun Wang graduated from The Johns Hopkins University with a Ph.D. degree in Chemistry. Jun joined Hubei University of Technology (Wuhan, China) in 2015 as a faculty in the Department of Biomedicine and Biopharmacology, and has been serving as a full professor and the director of the International Joint Research Center for Redox Biology Theory & Application of Hubei Province. Dr. Wang has published more than 50 peer-reviewed research papers in fundamental and translational studies of redox biology & medicine (h-index = 16), and served as a reviewer or editorial board member for several academic journals, including Inflammation, Journal of Alzheimer's Disease, Free Radical Biology & Medicine, Nitric Oxide, Journal of Biological Chemistry, EBioMedicine, Expert Opinion on Pharmacotherapy.

DDAH1, a key neuroprotective player, promotes neurogenesis and neural repair after cerebral ischemia insults

Yuming Zhao (肇玉明)

Department of Pharmacology, School of Basic Medical Sciences, Capital Medical University, Beijing, China

Email: yumingzhao@ccmu.edu.cn

Abstract

Choline acetyltransferase (ChAT)-positive neurons in neural stem cell (NSC) niches can evoke adult neurogenesis and restore impaired brain function after injury, such as acute ischemia stroke (AIS). However, the relevant mechanism by which ChAT+ neurons develop in NSC niches still remains poorly understood. Our RNA-seq analysis revealed that dimethylarginine dimethylaminohydrolase1 (DDAH1), a hydrolase for asymmetric dimethylarginine (ADMA), regulated genes responsible for the synthesis and transportation of ACh (e.g. Chat) post stroke insults. As expected, DDAH1 was clinically elevated in the peripheral blood of AIS patients which was positively correlated with AIS severity. By comparing the results among DDAH1 general knockout (KO) mice, transgenic (TG) mice and wild-type (WT) mice, we discovered that DDAH1 upregulated the proliferation and neural differentiation of NSCs in the subgranular zone (SGZ) under ischemic insults. As a result, it may promote cognitive and motor function recovery against the stroke impairments, while these neuroprotective activities are dramatically suppressed by NSC-specific conditional knockout of DDAH1 in mice.

Short CV

Dr ZHAO is the Associate Professor in Department of Pharmacology, School of Basic Medical Sciences, capital medical university, China. In Year 2005, she received the PhD degree from Chinese Academy of Medical Sciences and Peking Union Medical College. Currently, her group has focused on the preclinical pharmacological study of the antioxidants and neuroprotectants against the neurodegenerative insults. As the first author or corresponding author, Zhao has published more than 40 papers in peer reviewed international journals (e.g. Acta Pharmaceutica Sinica B, Free Radical Biology and Medicine, and Phytomedicine).

A physiological role of H_2O_2 in sleep homeostasis

Danqian Liu (刘丹倩)

Center for Excellence in Brain Science and Intelligence Technology (Institute of Neuroscience), Chinese Academy of Sciences, China

Email: dqliu@ion.ac.cn

Abstract

Sleep is essential for animal survival and health, and one proposed fundamental function of sleep is to combat oxidative stress. Yet, the relationship between sleep and reactive oxygen species (ROS) in the mammalian brain remains unclear. Here we show that in mice, sleep deprivation caused an overall brain ROS accumulation, with stronger increases in sleep regulating regions. By real-time imaging of intracellular H_2O_2 across sleep-wake cycles, we found that cytosolic but not mitochondrial H_2O_2 in key sleep neurons regulates sleep initiation. Elevating H_2O_2 optogenetically or chemogenetically in these neurons enhances sleep generation, while reducing intracellular H_2O_2 by overexpressing antioxidant enzyme suppresses sleep. These results highlight a physiological role for H_2O_2 in sleep homeostasis and uncover a feedback mechanism that triggers sleep for antioxidant protection.

Short CV

Liu Danqian got her bachelor's degree from the University of Science and Technology of China (USTC) in 2010. In 2016, she completed her Ph.D. at the Institute of Neuroscience, Chinese Academy of Sciences, studying synaptic plasticity underlying fear memory. From 2016 to 2020, she got her postdoctoral training at the University of California, Berkeley. Since 2020, Danqian is a principal investigator at the Center for Excellence in Brain Science and Intelligent Technology, Chinese Academy of Sciences. Her main researches focus on the functions of sleep in maintaining cellular homeostasis in the brain.

NRF2 translocation from dendrites to nucleus in glutamatergic pyramidal neurons induced by uncoupling of post-synaptic neuronal nitric oxide synthase via calcium influx through NMDAR

Ishii Tetsuro

University of Tsukuba, Japan

Email: ishiitetsuro305@gmail.com

Abstract

The transcription factor NRF2 plays a key role in maintaining high glutathione (GSH) levels in cells. In neurons, NRF2 is thought to control expression of the Na+-dependent amino acid transporter EAAT3, which takes up glutamate and cysteine, and γ-glutamyl-cysteine ligase for GSH synthesis. Hippocampal pyramidal glutamatergic neurons express both neuronal and endothelial nitric oxide synthases (nNOS and eNOS), and nitric oxide (NO) is important in potentiation of synaptic transmission. However, under synaptic depression, post-synaptic nNOS uncouples following glutamate stimulation of NMDA receptors to induce calcium influx. Subsequent reactive oxygen and nitrogen species generation would lead to GSH consumption. Uncoupled NOS-derived superoxide is converted to hydrogen peroxide (H_2O_2) via superoxide dismutase, and we previously proposed mechanisms for NRF2 nuclear translocation by low levels of hydrogen peroxide (Ishii T et al., Free Radic Biol Med (2022) 191: 191-202). The scaffolding protein PSD-95 binds nNOS in the post-synaptic membrane, while caveolin-1 tethers NRF2 in peri-synaptic lipid rafts. H_2O_2-activated ERK and p38 MAPKs, and calcium-activated PKC cooperate in membrane translocation and activation of the GSH sensor neutral sphingomyelinase 2 to generate the signaling molecule ceramide. Ceramide in turn activates the PKCζ/Casein kinase 2 signaling pathway to phosphorylates NRF2. ERK and cyclin-dependent kinase 5 phosphorylate NRF2 to induce a structural change by prolyl cis/trans isomerase Pin1 association to facilitate binding with importins. Subsequently, the dynein motor complex carries the NRF2 signaling complex toward nuclear pores along microtubules (Ishii T et al., Antioxidants (2023) 12:274).

Key words: NRF2, nitric oxide, superoxide, neuronal NO synthase, nuclear translocation, glutamate

Peroxynitrite reduces Treg cell expansion and function by mediating IL-2R nitration and aggravates multiple sclerosis pathogenesis

Meiling Wu (吴美玲)

The University of Hong Kong, China

Email: wumeilingcrow@hotmail.com

Abstract

T-helper 17 cells and regulatory T cells (Treg) are critical regulators in the pathogenesis of multiple sclerosis (MS) but the factors affecting Treg/Th17 balance remains largely unknown. Redox balance is crucial to maintaining immune homeostasis and reducing the severity of MS but the underlying mechanisms are unclear yet. Herein, we tested the hypothesis that peroxynitrite, a representative molecule of reactive nitrogen species (RNS), could inhibit peripheral Treg cells, disrupt Treg/Th17 balance and aggravate MS pathology by inducing nitration of interleukin-2 receptor (IL-2R) and down-regulating RAS/JNK-AP-1 signalling pathway. Experimental autoimmune encephalomyelitis (EAE) mouse model and serum samples of MS patients were used in the study. We found that the increases of 3-nitrotyrosine and IL-2R nitration in Treg cells were coincided with disease severity in the active EAE mice. Mechanistically, peroxynitrite-induced IL-2R nitration down-regulated RAS/JNK signalling pathway, subsequently impairing peripheral Treg expansion and function, increasing Teff infiltration into the central nerve system (CNS), aggravating demyelination and neurological deficits in the EAE mice. Those changes were abolished by peroxynitrite decomposition catalyst (PDC) treatment. Furthermore, transplantation of the PDC-treated-autologous Treg cells from donor EAE mice significantly decreased Th17 cells in both axillary lymph nodes and lumbar spinal cord, and ameliorated the neuropathology of the recipient EAE mice. Those results suggest that peroxynitrite could disrupt peripheral Treg/Th17 balance, and aggravate neuroinflammation and neurological deficit in active EAE/MS pathogenesis. The underlying mechanisms are related to induce the nitration of IL-2R and inhibit the RAS/JNK-AP-1 signalling pathway in Treg cells. The study highlights that targeting peroxynitrite-mediated peripheral IL-2R nitration in Treg cells could be a novel therapeutic strategy to restore Treg/Th17 balance and ameliorate MS/EAE pathogenesis. The study provides valuable insights into potential role of peripheral redox balance in maintaining CNS immune homeostasis.

Key words: Peroxynitrite, Nitration, IL-2R, Experimental autoimmune encephalomyelitis, Multiple sclerosis

ROMO1 shields the mitochondrial cysteinome from oxidations in diseases and aging

Xianhua Wang (王显花)

College of Future Technology, Peking University, China

Email: xianhua@pku.edu.cn

Abstract

Reactive thiols of proteinaceous cysteines are vital to cell biology by serving as sensor, effector and buffer of environmental redox fluctuations. Being the major source as well as the prime target of reactive oxygen species (ROS), the mitochondrion confronts great challenges in preserving its thiol pool. Here we identify ROS modulator 1 (ROMO1), a small inner mitochondrial membrane protein, as a master thiol-protector of the mitochondrial cysteinome. Being redox sensitive and reactive, ROMO1 shields functional thiols by scavenging ROS and forming intermolecular disulfides, thereby preventing irreversible thiol oxidations. Such ROMO1-mediated thiol protection exerts extensively beneficial effects on mitochondria, such as promoting energy metabolism and Ca2+ uniport while inhibiting vicious membrane permeability transition. Importantly, ROMO1 not only confers strong cardiac protection against oxidative injuries, but also reverses mitochondrial cysteinome oxidations in multiple organs and retards their functional declines in aging. These findings unravel an exquisite thiol-protection mechanism of the mitochondrial cysteinome, and mark ROMO1 as a potential target for combating oxidative stress and improving healthspan.

Key words: ROMO1, cysteine oxidations, mitochondria

Short CV

Dr. Xianhua Wang is an investigator of College of Future Technology, Peking University. She received her bachelor and Ph.D degrees in biochemistry and molecular biology from College of Life Sciences of Peking University, China, followed by postdoctoral training in Institute of Molecular Medicine, Peking University. Her research focuses on mitochondrial protection and mitochondrial signal transduction with the aid of cutting age *in vivo* mitochondrial imaging technique.

Alox15/15-HpETE Aggravates Myocardial Ischemia-Reperfusion Injury by Promoting Cardiomyocyte Ferroptosis

Xu Zhang (张栩)

Department of Physiology and Pathophysiology, Tianjin Medical University, China

Email: xuzhang@tmu.edu.cn

Abstract

Myocardial ischemia-reperfusion (I/R) injury causes cardiac dysfunction to myocardial cell loss and fibrosis. However, the time point at which the various modes of cell death occur after reperfusion injury and the mechanisms underlying ferroptosis regulation in cardiomyocytes are still unclear. We found that apoptosis and necrosis occurred in the early phase of I/R injury, and that ferroptosis was the predominant form of cell death during the prolonged reperfusion. We demonstrated that Alox15 expression was specifically increased in the injured area of the left ventricle below the suture and colocalized with cardiomyocytes. Furthermore, myocardialspecific knockout of Alox15 in mice alleviated I/R injury and restored cardiac function. 15-Hydroperoxyeicosatetraenoic acid (15-HpETE) was identified as a trigger for cardiomyocyte ferroptosis. We explored the mechanism underlying its effects and found that 15-HpETE promoted the binding of Pgc1α to the ubiquitin ligase ring finger protein 34, leading to its ubiquitin-dependent degradation. Consequently, attenuated mitochondrial biogenesis and abnormal mitochondrial morphology were observed. ML351, a specific inhibitor of Alox15, increased the protein level of Pgc1α, inhibited cardiomyocyte ferroptosis, protected the injured myocardium, and caused cardiac function recovery.

Key word: 15-HpETE , Ferroptosis, ML351, Myocardium

Short CV

Xu Zhang, PhD, professor of Tianjin Medical University.

Mainly engaged in the research of "Pathophysiological Role and Regulatory Mechanisms of Bioactive Lipid Molecules".

Papers published in journals including Circulation, Circulation Research, Eur Respir J, Nature Communication, etc.

The Mechanisms of Plasma-Activated Solutions in Treating Atopic Dermatitis

Yan Zheng (郑焱)

Department of Dermatology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Email: zenyan66@126.com

Abstract

Cold atmosphere plasma has been applied to many diseases and has been extensively studied in dermatology in recent years, addressing conditions such as wound healing, psoriasis, dermatitis, and vitiligo. Compared to direct plasma treatment, plasma-activated solutions (PAS) offer several advantages, including enhanced safety, better portability, higher patient acceptance, and greater convenience for application in sensitive areas, such as skin folds. These benefits have brought PAS increasing attention in the field.

Atopic dermatitis (AD) is a widespread chronic inflammatory skin condition that remains incurable, creating an urgent need for alternative therapies or daily management strategies with fewer side effects. Therefore, in this work we explore the potential of PAS as a promising treatment option for AD.

Our *in vivo* experiments demonstrated the therapeutic efficacy of PAS in a mouse model of AD, including its effectiveness in alleviating AD-like symptoms, reducing inflammatory markers, and reducing mast cell and macrophage infiltration. These benefits were linked to the activation of the antioxidant molecule Nrf2. Further, in vitro experiments using THP-1-derived macrophages showed that PAS reduced ROS levels and regulated cytokine expression in TNF-α/IFN-γ-stimulated keratinocytes and LPS-stimulated M1 macrophages. PAS also upregulated antioxidant stress molecules like Nrf2, HO-1, NQO1, and PPAR-γ in both cell types.

Overall, PAS demonstrated potent therapeutic potential for AD without notable side effects. Our research provided a promising approach to AD treatment and may open a novel avenue for treating.

Short CV

Department of dermatology, Xi'an Jiaotong University, Shaanxi, China, Professor

Department of dermatology, the First Affiliated Hospital of Xi'an Jiaotong University, Shaanxi, China, Director

Research Interests: Scientific research: pathogenesis of psoriasis and skin cancers; Clinical aspects: treatment of psoriasis and atopic dermatitis; pathological diagnosis of rare skin diseases; laser cosmetic treatment of skin

Symposium-7(S7)

Redox signaling in organelles/cell fate/development/reproduction

Chair: Dongyun Shi (施冬云)

Fudan University, China

Email: dyshi@fudan.edu.cn

Short CV

Dr. Dongyun Shi received his BS and MS from Fudan University and PhD of Biochemistry and Cell Biology from Kings College, University of London, UK. Currently, she is a professor in the Department of Biochemistry, School of Basic Medicine, Fudan University, at Shanghai, China. Dr. Shi's research interests include the molecular and cellular mechanisms of reactive oxygen species in regulating metabolic diseases, focusing on the redox modulation of the metabolism in tumors and diabetes. She was selected as Pujiang Talent of Shanghai, and won the second prize of the Natural Science Award of the Ministry of Education of the People's Republic of China.

Airborne PM2.5-induced oxidative stress aggravates neurotoxicity in olfactory bulb

Wenjun Ding (丁文军)

Laboratory of Environment and Health, College of Life Sciences, University of Chinese Academy of Sciences, Beijing, China

Email: dingwj@ucas.ac.cn

Abstract

Recent epidemiological studies have shown that exposure to atmospheric fine particulate matter (PM2.5) is associated with various central nervous system (CNS) diseases, including Alzheimer's disease and Parkinson's disease, etc. PM-induced microglia activation, neuroinflammation and oxidative stress are critical to the neurodegenerative diseases in the CNS. However, the cellular and molecular mechanisms by which PM2.5 induces neurotoxicity are not well understood. In our study, we found that PM2.5 entered the brain via olfactory pathway. PM2.5 significantly increased the concentrations of metal elements in mice olfactory bulb (OB). Compared with the controls, PM2.5 triggered oxidative stress and activated microglia in mice OB. Moreover, the release levels of glutaminase-containing EVs (40-200 nm) and the number of apoptotic cells were significantly increased following PM2.5 exposure. Furthermore, nuclear factor erythroid 2-related factor 2 (Nrf2) deficiency resulted in lower levels of antioxidant enzymes, greater induction of oxidative stress, microglia activation, inflammation and nuclear factor kappa B (NF-κB) activation in PM2.5-treated OBs. Taken together, glutaminase-containing EVs are crucial neurotoxic factors released by PM2.5-activated microglia. Nrf2-mediated defenses against oxidative stress will help develop new strategies for the prevention and treatment of diseases associated with airborne PM2.5 pollution.

Key words: PM2.5, oxidative stress, olfactory bulb, glutaminase, neuroinflammation, microglia, extracellular vesicles

Short CV

Wenjun Ding, Professor, Vice Dean, College of Life Sciences, University of Chinese Academy of Sciences (UCAS). At UCAS, he established and is leading a research group "Environment and Health". This group is focusing on the toxicological implications of Urban airborne fine particulate matter: sources, chemical composition, and possible underlying mechanism, especially cardiopulmonary diseases attributable to indoor and/or outdoor air pollution.

Deciphering umbilical cord blood hematopoietic stem/progenitor cell alterations in alpha-thalassemia using single-cell transcriptomics

Yanlin Ma (马燕琳)

Department of Reproductive Medicine, the First Affiliated Hospital of Hainan Medical University, Haikou City, China

Email: mayl1990@foxmail.com

Abstract

Alpha-thalassemia represents one of the most globally widespread monogenic disorders. The main pathological features of α-thalassemia include ineffective erythropoiesis, hemolysis, and iron overload. Although the pathophysiology of α-thalassemia has been extensively studied in many aspects, it remains unclear how α-thalassemia affects the differentiation process of hematopoietic stem/progenitor cells (HSPCs). Here, we isolated CD34+ HSPCs from the umbilical cord blood of fetuses with α-thalassemia and conducted single-cell RNA sequencing. After stringent quality control, a total of 49,263 CD34+ HSPCs were included in downstream analysis. Based on known marker genes, 16 different cell clusters were annotated. Pseudotime analysis showed that CD34+ HSPCs from α-thalassemia and control exhibited similar differentiation trajectories, but there were differences in the number of cells differentiating along these paths. Compared to the control group, the MEP cell and Mk P cell proportion were significantly elevated in α-thalassemia, while the proportion of pro-B cells was generally reduced, with the differences being statistically significant.

We assessed the transcriptomic changes in each cell subtype in the thalassemia group and found that most of the differentially expressed genes were downregulated. Gene set enrichment analysis of these DEGs revealed significant enrichment in several key biological processes and signaling pathways, including positive regulation of GTPase activity, the PI3K-AKT signaling pathway, G protein-coupled receptor signaling pathway, and TGF-β receptor signaling pathway. The expression of genes associated with these processes was significantly reduced, suggesting that these biological functions may be suppressed or weakened. Moreover, in the HSC/MPP cell subtype, there was an observed increase in oxidative phosphorylation. An increase in oxidative phosphorylation is often accompanied by a rise in reactive oxygen species (ROS) levels, and excessive ROS can trigger oxidative stress. Oxidative stress can lead to cellular damage, impair cell function, and subsequently affect the self-renewal and differentiation potential of HSCs. These findings suggest that increased oxidative phosphorylation and ROS production may be key mechanisms underlying impaired HSC function and disrupted intracellular homeostasis in thalassemia. Elevated ROS levels may further exacerbate oxidative stress in

thalassemia patients, thus impacting overall hematopoiesis and normal immune system development.Further differentiation trajectory analysis revealed that, compared to the control group, the HSC/MPP cell population in α-thalassemia showed a marked increase in differentiation toward MEP.

In pro-B cells of α-thalassemia, the expression of genes associated with programmed cell death, such as BAX and BAD, was significantly increased. The activation of the TP53 signaling pathway was accompanied by the upregulation of a series of direct effector genes, including CHEK1, PCNA, and PRMT1. Additionally, GO analysis indicated that pathways related to B cell proliferation and immature B cell differentiation were significantly downregulated in α-thalassemia, suggesting that pro-B cell apoptosis is significantly increased, and their differentiation process is severely impaired. These defects lead to a significant reduction in pro-B cell numbers, which may ultimately contribute to abnormal immune system function in α-thalassemia patients.

For the first time, we utilized single-cell transcriptomics to reveal the altered transcriptomic characteristics of CD34+ HSPCs in the umbilical cord blood of α-thalassemia patients. We discovered significant differences in the differentiation fate of HSC/MPP between α-thalassemia patients and controls. This differentiation tendency is likely a compensatory response by the patients to ineffective erythropoiesis and to address the insufficiency of red blood cell production in their bodies.

Key words: α-thalassemia, hematopoietic stem and progenitor cells, single-cell RNA sequencing, lineage differentiation bias;ROS

Short CV

Ma Yanlin is a distinguished expert recognized by the National Health Commission as an Outstanding Young and Middle-aged Expert for her significant contributions. She is also a recipient of the State Council Special Allowance and holds the title of Second-level Professor. Ma has long been engaged in clinical and laboratory work in the fields of reproductive medicine and genetic counseling.

Identification of druggable and redox vulnerabilities in cancer

Liron Bar-Peled

Harvard Medical School Department of Medicine, USA

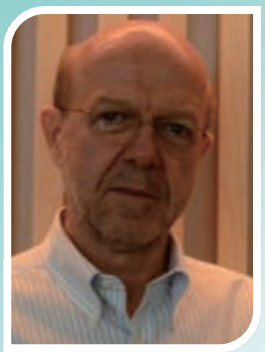
Email: lbar-peled@mgh.harvard.edu

Abstract

Multiple chemotherapies are proposed to cause cell death in part by increasing the steady-state levels of cellular reactive oxygen species (ROS). However, for most of these drugs exactly how the resultant ROS function and are sensed is poorly understood. In particular, it's unclear which proteins the ROS modify and their roles in chemotherapy sensitivity/resistance. To answer these questions, we examined 11 chemotherapies with an integrated proteogenomic approach identifying many unique targets for these drugs but also shared ones including ribosomal components, suggesting one mechanism by which chemotherapies regulate translation. We focus on CHK1 which we find is a nuclear H_2O_2 sensor that promotes an anti-ROS cellular program. CHK1 acts by phosphorylating the mitochondrial-DNA binding protein SSBP1, preventing its mitochondrial localization, which in turn decreases nuclear H_2O_2. Our results reveal a druggable nucleus-to-mitochondria ROS sensing pathway required to resolve nuclear H_2O_2 accumulation, which mediates resistance to platinum-based chemotherapies in ovarian cancers.

Short CV

Liron received his Bachelor of Science degree in Biochemistry from the University of Georgia in 2004. Liron received his PhD in Biology from the Massachusetts Institute of Technology, where he used advanced cellular and molecular techniques to uncover how nutrients are sensed by the mTORC1 pathway in the laboratory of David Sabatini. In 2013 as a Damon Runyon Postdoctoral fellow, he joined the laboratory of Ben Cravatt at the Scripps Research Institute to understand how cancer cells respond to oxidative stress. Employing chemical, proteomic and biochemical approaches, Liron revealed new druggable components of the NRF2 antioxidant response pathway uncovering new mechanisms by which NRF2 regulates metabolic pathways. In early 2019, Liron joined the Center for Cancer Research at the Massachusetts General Hospital and the Department of Medicine at Harvard Medical School. He is currently an Associate Professor of Medicine in Biological and Biomedical Sciences.



An endoplasmic reticulum-based model of intercellular redox communication

Francisco Laurindo

University of São Paulo, Brazil

Email: francisco.laurindo@hc.fm.usp.br

Short CV

Francisco R. M. Laurindo graduated from the University of São Paulo School of Medicine, São Paulo, Brazil and underwent training in basic research in Physiology and Pharmacology at the Uniformed Services University of the Health Sciences, in Bethesda, MD, USA. Back to the Heart Institute, USP, he started an investigative research track on redox vascular biology, materializing into the Vascular Biology Laboratory at this institution, which he leads since 2008. His major research interests are mechanisms and regulation of oxidant and thiol signaling in vascular cells and their physiological implications for vessel remodeling in disease. Dr. Laurindo has authored or co-authored over 185 publications in peer-reviewed journals, and supervised over 25 PhD students and 25 post-doctoral fellows, in addition to several undergraduate trainees. Since 2008 (until present), he is the Vice-coordinator of Cepid-Fapesp Redoxoma, a large network project. He is a member of the Brazilian Academy of Sciences since 2012 and a member of its Board of Directors from 2016-2022; a member of Fapesp Research Agency Advisory Committee in Health Sciences from 2008-2024. He served as Council Member of the SfRBM (Soc. for Redox Biol Med) from 2010-2014, President-elect from 2020-22 and is current SfRBM President since 2022. He belongs to the Editorial Boards of Free Radical Biology and Medicine, Clinical Science and Circulation Research. He was vice-chair (2014) and chair (2016) of the Gordon Research Conference on Nox Family NADPH Oxidases.

Apoptotic Effect of Terfenadine, a Histamine H1 Receptor Antagonist, and Terfenadine-loaded Human Serum Albumin Nanoparticles in Colorectal Cancer and Glioblastoma Cells

Kyung-Soo Chun

College of Pharmacy, Keimyung University, Daegu, 42601, Korea

Email: chunks@kmu.ac.kr

Abstract

Terfenadine is a second-generation histamine H1 receptor antagonist initially used for treatment of allergy. However, it was withdrawn from market due to serious adverse effects of the drug. Recently, we investigated that terfenadine exhibited marked antitumor effects against HCT116 colorectal cancer cells by inducing apoptosis via cleavage of caspase and PARP and release of cytochrome C. Moreover, terfenadine treatment decreased the phosphorylation of STAT3 and downregulated the expression of its target gene products such as cyclin D1, cyclin D2, cyclin D3 and survivin. In addition, terfenadine treatment led to aberrant reactive oxygen species generation (ROS) in HCT116 cells which could trigger apoptosis. Moreover, terfenadine showed prominent antitumor effects against U87MG glioblastoma cells. Addressing the challenge for revival of terfenadine in clinic, we attempted to develop human serum albumin (HSA) based nanoplatform incorporating terfenadine as payload which is speculated to minimize the adverse effects associated with the drug and increase the cell permeability in cancer cells. Indeed, terfenadine-loaded HSA-NPs (T-HSA-NPs) exhibited desired particle characteristics along with sustained release pattern. Incubation of cells with T-HSA-NPs showed enhanced cellular internalization, and higher cytotoxic effects in U87MG and HCT116 cells as compared to the free drug. In conclusion, our results illuminate on the potential of T-HSA-NPs for chemotherapy and represent efficient approach to enhance the permeability of terfenadine across blood brain barrier which is a key to the treatment of brain tumors.

<Baniya M.K.et al. Front. Pharmacol. 2024;15:118266.>

Short CV

ADDRESS: College of Pharmacy, Keimyung University, South Korea

EDUCATION: Ph.D. in Pharmacy, Seoul National University, Seoul, Korea, 2004

RESEARCH/PROFESSIONAL EXPERIENCE:

2011 – Present, Professor, College of Pharmacy, Keimyung University

2004 – 2011, Research Fellow, Laboratory of Toxicology and Pharmacology, NIEHS/NIH, Research Triangle Park, NC, USA

MAJOR: Molecular Toxicology, Cancer Biology

Symposium-8(S8)

Redox and aging ② “Targeting Redox and Mitochondria to delay aging and prevent age-related diseases”Forum

Chair: Yong Zhang (张勇)

Tianjin Key Laboratory of Exercise, Physiology and Sports Medicine, Tianjin University of Sport, Tianjin, China

Email: yzhang@tjus.edu.cn

Short CV

Dr. Yong Zhang got his BS from Hubei University in Biology and his PhD from Beijing Sports University, majoring in exercise physiology. He is a professor of Tianjin University of Sport and adjunct professor of Beijing Sport University and Xi'an Jiaotong University, and was International Visiting Professor of Southern Cross University, Australia. Prof. Zhang's Research interest is Cellular and Molecular Exercise Physiology: 1) Exercise-induced Oxidative Stress and Mitochondrial Biology, and 2) Mitochondrial Homeostasis Regulation and Integrative Physiology of Exercise. He has published more than 100 papers on exercise on health.

Redox regulation of mitophagy by targeting PINK1

Hanming Shen (沈汉明)

Faculty of Health Sciences, University of Macau, Macau, China

Email: hmshen@um.edu,mo

Abstract

Mitophagy is a selective form of autophagy for clearance of damaged mitochondria via the autophagy-lysosome pathway. Among various mitophagy regulators, PINK1, a protein kinase, and Parkin, an E3 ligase, are two critical players, with important implications in neurodegenerative disorders such as Parkinson's disease (PD). In our recent studies, we focus on the upstream regulatory mechanisms of PINK1, including the following aspects: (1) Via a whole genome CRISPR-Cas9 screening, we identified glucose-6-phosphate dehydrogenase (G6PD), a key enzyme in glycolysis antioxidant defense mechanism, as an important positive regulator of mitophagy via direct interaction and stabilization of PINK1; (2) Establishing the regulatory function of reactive oxygen species (ROS) on mitophagy: H_2O_2 is capable of impairing the mitophagy process via PARP1 activation and PARylation of key mitophagy machinery. Our results thus provide a deeper insight into the molecular mechanisms in control of PINK1, the guardian of mitochondria and lay foundation for development of novel interventional strategies in PINK1- and mitophagy-related human diseases such as neurodegeneration and cancer.

Key words: Mitophagy, PINK1, G6PD, ROS, PARylation

Short CV

Dr. Han-Ming Shen is currently a Chair Professor and Associate Dean (Teaching), Faculty of Health Sciences, University of Macau, and a visiting Professor, Yong Loo Lin School of Medicine, National University of Singapore (NUS). He received his Bachelor of Medicine (1985), Master of Medicine (1988) and PhD (1996) from Zhejiang Medical University and NUS, respectively. He also received his postdoc training in National Cancer Institute (NCI), National Institutes of Health (NIH). His research is focused on the autophagy-lysosome pathway, mitophagy, as well as on glucose metabolism in cancer cell biology. Dr. Shen has published more than 250 papers, with more than 44,000 citations and H-index at 104 (Google scholar). Currently, he serves as the Associate Editor for Autophagy, and as member of editorial board for several other journals such as Life Metabolism, Burns & Trauma and Aging Cell.

NAD$^+$ dependent UPR^{mt} activation underlies intestinal aging caused by mitochondrial DNA mutations

Xingguo Liu (刘兴国)

Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, China

Email: liu_xingguo@gibh.ac.cn

Abstract

Aging in mammals is accompanied by an imbalance of intestinal homeostasis and accumulation of mitochondrial DNA (mtDNA) mutations. However, little is known about how accumulated mtDNA mutations modulate intestinal homeostasis. We observe the accumulation of mtDNA mutations in the small intestine of aged male mice, suggesting an association with physiological intestinal aging. Using polymerase gamma (POLG) mutator mice and wild-type mice, we generate male mice with progressive mtDNA mutation burdens. Investigation utilizing organoid technology and *in vivo* intestinal stem cell labeling reveals decreased colony formation efficiency of intestinal crypts and LGR5-expressing intestinal stem cells in response to a threshold mtDNA mutation burden. Mechanistically, increased mtDNA mutation burden exacerbates the aging phenotype of the small intestine through ATF5 dependent mitochondrial unfolded protein response (UPRmt) activation. This aging phenotype is reversed by supplementation with the NAD$^+$ precursor, NMN. Thus, we uncover a NAD$^+$ dependent UPRmt triggered by mtDNA mutations that regulates the intestinal aging.

Key words: NAD, mitochondrial DNA, Aging, redox state, mitochondrial unfolded protein response

Short CV

Professor Xingguo Liu, was honored as "Distinguish Youth Foundation" of National Natural Science Foundation, Chief Scientist of the National Key Research and Development Program of China, 1st finisher of the first prize of the Guangdong Science and Technology Award in Natural Science, The Shulan Medicine Youth Award by the Academician Shusen Lanjuan Talent' Foundation, The Ying Ding Science and Technology Award, "2016 Stem cell Young Investigator Award" from Chinese Society for Cell Biology and "Young Bioenergeticist Award" of the International Biophysical Society. He is the Executive Editor of Science Bulletin, the council member of the Asian Society for Mitochondrial Research and Medicine, and the council member of the Biophysical Society of China. Dr. Liu has published more than 80 papers, which have been cited for more than 6000 times. Since 2015, he has published 32 research papers as corresponding author (4 IF>20, 22 IF>9), such as Cell Metabolism (2016,2018, 2024), Nature Metabolism, Nature Structural & Molecular Biology, Nature Communications (2022,2024), Science Advances (2019, 2022), Advanced Science, Hepatology. Among his papers, 3 were recommended by F1000, 9 were chosen as cover, and his findings have been listed in 17 books such as Encyclopedia of Biological Chemistry. He obtained 10 authorized patents (including one PCT). Dr. Liu has been the invited speaker in Keystone Symposia.

Truncated oxidized phospholipids mediate synchronized ferroptosis and contribute to acute kidney injury

Quan Chen (陈佺)

State Key Laboratory of Medicinal Chemical Biology, College of Life Sciences, Nankai University, Tianjin 300071, China.

Email: chenq@nankai.edu.cn

Abstract

Synchronized ferroptosis is suggested to play a significant role in nephron loss during acute kidney injury (AKI). However, the underlying mechanisms mediating synchronized ferroptosis in renal tubular injury remain unclear. Our study reveals that truncated oxidized phospholipids and platelet-activating factor (PAF) serve as mediators of synchronized ferroptosis, contributing to the pathogenesis of acute kidney injury (AKI). PAF initiates biomembrane permeabilization and triggers cell death in neighboring cells. PAF-acetylhydrolase (II) (PAFAH2), a phospholipase A2 (PLA2) family enzyme that specifically removes truncated acyl chains from phospholipids, along with PAF-specific antibodies that bind and neutralize PAF, effectively suppressed synchronized ferroptosis. Genetic or pharmacological inhibition of PAFAH2 led to increased PAF production, which augmented PAF-mediated synchronized ferroptosis and exacerbated ischemia/reperfusion (I/R)-induced AKI. Our findings uncover a novel mechanism underlying synchronized ferroptosis and propose a promising therapeutic strategy for the intervention of acute kidney injury (AKI).

Short CV

Dr. Quan Chen is the Professor and Director of Life Science in Nankai University (Tianjin, China) and Director of State Key Laboratory of Medicinal Chemical Biology. He works on the role of mitochondria in apoptosis, the molecular regulation of mitochondrial autophagy and the role of mitochondrial dysfunction in the occurrence of neurodegenerative diseases such as Alzheimer's disease, Parkinson's syndrome as well as cancer stem cells in tumorigenesis and metastasis. He serves on the editorial boards of JBC, Cell Research, Cell Death and Disease and Chinese Science journals. Professor Chen has received the American Association for Cancer Research (AACR-AFLAC) Young Scholar Award for Cancer Research, the 4th Tan Jiazhen Life Science Award Innovation Award, and the National Outstanding Scientific and Technological Worker. The research interests in Dr. Chen's laboratory: research apoptosis signal transduction and mitochondrial biology, focus on the role of mitochondria in apoptosis signaling, the role of apoptosis in tumorigenesis; analyze the molecular mechanisms of mitochondrial dynamic changes and quality control and theirs' function in neurodegenerative diseases; screen natural small molecule compound by targeting of key molecules of mitochondria and apoptosis; research on cancer stem cells.

NAD^+-dependent enzymes in health and disease: Our key findings on NADH-ubiquinone oxidoreductase in diabetic pancreas

Liang-Jun Yan

University of North Texas Health Science Center, Fort Worth, TX, USA

Email: liang-jun.yan@unthsc.edu

Abstract

It has been established that there is an oversupply of NADH in diabetes which can lead to cellular redox imbalance. As mitochondrial complex I is the major site accepting NADH electrons, how complex I responds to this redox imbalance and the consequences of this response have not been investigated, particularly in the pancreas. Therefore, we aimed to study the effects of NADH/NAD^+ redox imbalance on complex I and mitochondria in diabetic pancreas. Materials and Methods: Type 2 diabetic animal models such as Zucker diabetic rat and db/db mouse were from Charles River. Type I diabetes was induced by streptozotocin injection in rats. Complex I activity was determined by native gel electrophoresis. NADH/NAD^+, ATP concentrations, and apoptosis were measured using commercially available kits, respectively. Lipid peroxidation, protein oxidation, and H_2O_2 levels were also measured. Results: Pancreatic mitochondrial complex I was found to be highly activated by diabetic hyperglycemia in both type I and type 2 diabetes. Moreover, while NADH content was increased, the levels of ATP levels was decreased. We also discovered that the effect of NADH/NAD^+redox imbalance on complex I leads to mitochondrial oxidative stress and cell death. Conclusion: Our study suggests that complex I hyperactivity in diabetic pancreas is involved in the pathogenesis of diabetes.

Key words: Redox imbalance, mitochondria, oxidative stress, diabetes, redox imbalance, NADH-ubiquinone oxidoreductase

Short CV

Education	1996, PhD, University of California-Berkeley
	1990, MS, Institute of Biophysics, Chinese Academy of Sciences
	1987, BS, Peking University
Postdoc	2000, Southern Methodist University, Dallas, Texas
Membership	International Society of Nephrology
	Society for Redox Biology and Medicine
	American Society for Biochemistry and Molecular Biology
	International Society for Neurochemistry
	American Association of Advancement of Science
	Golden Bear Life Member-Cal Alumni Association, UC Berkeley
Positions	Tenured Professor, Pharmaceutical Sciences
Department/Affiliation	Pharmaceutical Sciences, College of Pharmacy
	Graduate School of Biomedical Sciences
	Institute for Aging and Alzheimer's disease Research

Education Program Involvement

Pharmacology and Medicinal Chemistry, PharmD; Pharmaceutical Sciences and Pharmacotherapy, PhD; Biomedical Sciences, PhD

Publications: https://www.ncbi.nlm.nih.gov/myncbi/1d7TqQRoGlw/bibliography/public/

Mitochondrial drug NAD^+ anti-aging strategy

Kanglin Wang (王康林)

Knature Bio-pharma Co., Ltd.

Email: wangkanglin@knb-pharma.com

Abstract

With the coming of aging population in the world, the incidence of aging-related diseases such as heart failure, neurodegenerative diseases, tumors, etc. will increase sharply day by day. As an important substance in mitochondria within intracellular, NAD^+ plays a variety of important roles in intracellular, involving multiple biological processes such as energy metabolism, DNA repair, signal transduction, antioxidant, immune regulation, and apoptosis.

Through cardiomyocyte models, Sprague Dawley(SD) rats models, beagles models, and other animal models, compared with Novartis's LCZ696, it was confirmed that NAD^+ has an obvious advantage in anti-heart failure function key indicators such as left ventricular ejection fraction(LVEF) and myocardial infarction area. 60 candidate patients performed one Investigator-initiated clinical trial， and researchers also confirmed that NAD^+ can improve key indicators such as NT-proBNP and LVEF value in the heart-failure candidates patients group. Through pre-clinical research, a registered clinical trial of NAD^+ was carried out and approved by China Food and Drug Administration. The maximum ramping dose of the clinical trial human phase I reached 800 mg daily. It shows that the security in clinical trial phase I is fairly safe.

Compared with Memantine, Cholinesterase inhibitors such as Donepezil, Galantamine, and Rivastigmine, NAD^+ effectively inhibits reactive oxygen species (ROS) generated by free radicals, and increases the expression levels of Superoxide dismutase (SOD) mRNA and glutathione (GSH) mRNA. It improves neuronal cell viability. In a chronic cerebral ischemia rat model, NAD^+ reduces ROS damage and neuroinflammatory response in mitochondria, showing obvious anti-neuro- degenerative disease functions.

Immune checkpoint inhibitor drugs such as PD-1/L1 are primary clinical drugs used for cancer patients. However, the clinical tumor immune response rate is relatively low, at 15-20%, and PD-1/L1 is ineffective for most cancer patients. Research has shown that when NAD^+ is used in combination with PD-1/L1, NAD^+ can significantly improve the immune response rate of PD1/L1 in liver cancer and pancreatic cancer SD rats models. The tumor immune response rate increased from 42.2% to 82.8% in liver cancer SD rats models and from 18.6% to 64.7% in pancreatic cancer SD rats models. An Investigator-initiated clinical trial of the combination of NAD^+ and PD1/L1 drug is currently underway.

Symposium-9(S9)

Redox and cancer, infection and immunity

Chair: Pingping Shen (沈萍萍)

Nanjing University, China

Email: ppshen@nju.edu.cn

Short CV

Nanjing University, Jiangsu, P.R.C	BS	1980-1984	Biology
Nanjing University, Jiangsu, P.R.C	MS	1987-1990	Biology
Nanjing University, Jiangsu, P.R.C	Ph.D	1997-2000	Biochemistry and Molecular Biology

2018- present, The Comprehensive Cancer Center, Nanjing Drum Tower Hospital

2011-2018 Head of Department, Department of Bioscience and Engineering, Jinling College, Nanjing University

2004-present PI, State Key Laboratory of Pharmaceutical Biotechnology, Nanjing University; Professor, School of Life Sciences, Nanjing University

2003-2007 Associate Dean, School of Life Sciences, Nanjing University

2002-2003 Visiting Professor, University of California at San Diego

The research interests of my research group is to investigate he reprogramming mechanisms of macrophages within inflammatory microenvironments and their implications for human diseases. With a longstanding history of exploring the precise functions of specific macrophage subsets in the progression and prognostic outcomes of inflammation-related diseases, including cancer and metabolic inflammation. Our research integrates immunology, cell biology, and molecular biology to delineate the signaling transduction cascades, identify associated key regulatory nodes in macrophage function, and elucidate the exact mechanism by which these key nodes contribute to macrophage differentiation and polarization of immune responses. My lab employs engineering strategies, such as intracellular domain (ICD) assembly, metabolic/genetic editing, and chemical intervention, to develop chimeric antigen receptor macrophages (CAR-M) for solid tumors and autoimmune diseases. Additionally, leveraging synthetic biology, we have developed an intelligent CAR-M technology platform that allows for controllable assembly and tunable activity, endowing CAR-M with the capability of recognizing target antigens and precise manipulation of intracellular functional modules. Concurrently, we are advancing studies to design and implement in situ reprogramming approaches for *in vivo* macrophage engineering and CAR-M self-assembly.

Homepage: https://biopharm.nju.edu.cn//rcdw/yjry/20191126/i53941.html

The role of redox metabolism in drug resistance of cancer therapy

Zigang Dong (董子钢)

Zhengzhou University, China

Email: dongzg@zzu.edu.cn

Abstract

Many targeted drugs for tumor therapy primarily focus on redox reaction metabolism. During this process, sensitivity and resistance to these targeted drugs occured. Resistance to paclitaxel poses a major obstacle in esophageal squamous cell carcinoma (ESCC) treatment. A better understanding of the mechanisms underlying paclitaxel resistance could help identify prognostic biomarkers and improved therapeutic strategies. In this study, we established a patient-derived xenograft (PDX) model of acquired paclitaxel resistance and used RNA-sequencing to identify galectin-1, encoded by LGALS1, as a key mediator of resistance. Integrative analysis of clinical data and physiological studies indicated that serum galectin-1 levels were elevated in resistant patients and correlated with treatment outcomes before and during taxane therapy. Importantly, exposing cells to serum from resistant patients resulted in increased paclitaxel resistance compared to serum from sensitive patients, which was closely associated with galectin-1 concentrations in the serum. The specific clearance of galectin-1 from resistant patient serum significantly restored paclitaxel sensitivity, and inhibiting galectin-1, through knockdown or the pharmacologic inhibitor OTX008, increased sensitivity to paclitaxel. Galectin-1 inhibition reduced the activity of β-catenin, thereby inhibiting stem cell properties induced by the Wnt/β-catenin pathway. Furthermore, galectin-1 regulated MDR1 transcription through increased nuclear accumulation of β-catenin, thus increasing resistance to paclitaxel. Combining OTX008 with clinical taxane formulations effectively reversed paclitaxel resistance in vitro and *in vivo*. Elevated galectin-1 levels thus serve as an indicator of response to paclitaxel therapy in ESCC, offering a therapeutic intervention strategy to overcome drug resistance.

Short CV

Professor Zigang Dong, who got his PhD from Mailman School of Public Health, Columbia University, worked as the Director of The Hormel Institute, University of Minnesota for a long period of time, and currently is serving as a vice president of Zhengzhou University as well as the director of School of Medicine. Professor Dong focuses on the pathogenesis and prevention of cancer and is a leading figure in the field of cancer chemoprevention in the world. As of now, he has published more than 500 papers on journals such as Nature, Nature Reviews Cancer, Nature Cell Biology, etc. The total citations of his papers exceed 40,000. He also serves as an editorial board member or associate editor of journals including Cancer Research. He co-lunched npj Precision Oncology with Nature Publishing Group.

Professor Dong has presided over 50 plus projects funded by NIH and NSFC. Honors and awards won by him include McKnight Presidential Professor(the highest honor of University of Minnesota), MERIT Award(NIH, 2008), Stars in Nutrition and Cancer Lecturer Award(American Institute for Cancer Research, 2012), Yellow River Friendship Award (Henan Provincial Government, 2014) , Outstanding Contribution Award in Cancer Research(Society of American Asian Scientists, 2016), Contribution Award for overseas Chinese (All-China Federation of Returned Overseas Chinese, 2020) and Award for International Cooperation on Science and Technology (Henan Provincial Government, 2020). In 2021, professor Dong was included in the list of the top 100,000 scientists in the world. He ranks third among clinical researchers in China's mainland and is high on the list of scientists in Henan province. His name is frequently present in the lists of most cited Chinese researchers and the top 2% global researchers.

Redox biology regulated by selenoproteins- significance for biological defense and its relation to cancer

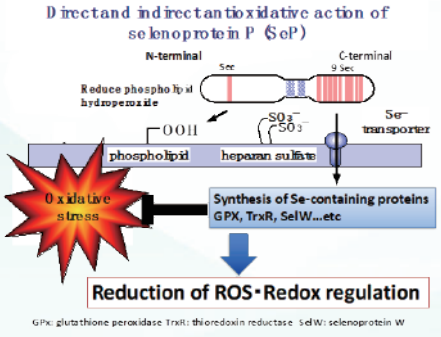
Yoshiro Saito

Laboratory of Molecular Biology and Metabolism, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, 980-8578, Japan

Email: yoshiro.saito.a8@tohoku.ac.jp

Abstract

"Selenoprotein" is a general term for proteins that contain the essential trace element selenium in the form of selenocysteine (Sec), and 25 types are known in humans. Sec is encoded by one of the stop codons "UGA" and is called the 21st amino acid that can be translated. Selenoproteins play a significant role in redox reactions in the body, and representative selenoproteins are glutathione peroxidase (GPX), which reduces and detoxifies peroxides, and thioredoxin reductase, which is related to redox regulation. Selenoprotein P (SeP), which exists in plasma, is mainly synthesized in the liver and transports selenium to the periphery tissues. SeP has 10 Sec residues in the molecule, with one Sec residue on the N-terminus possessing GPX-like activity and nine Sec residues on the C-terminus functioning in selenium transport. In addition to its antioxidant action, SeP maintains cellular selenoproteins and plays an important role in antioxidant defense and redox regulation in the body (See Figure below). On the other hand, it has become clear that dysregulation of SeP expression is involved in various diseases such as diabetes and cancer. In this presentation, I will show the protective effect of SeP against electrophiles, which has been newly discovered as a biological function of SeP. Further, I introduce the latest findings on the relationship with severe brain cancer glioblastoma, associated with overexpression of SeP. In this lecture, I want to discuss the dual nature of selenoproteins from the view of redox biology.



Key words: Selenoprotein, Metabolism, Electrophile, Glioblastoma

Short CV

Yoshiro Saito, a professor at Tohoku University, received PhD from Hokkaido University in 2001 for his research on the structure and function of selenoprotein P. He became a postdoctoral researcher at AIST in 2002 and worked on oxidative stress biomarkers and their cellular responses. He researched oxidative stress and disease at Doshisha University since 2008 and has been in his current position since 2018. He has published 138 original papers with an H-index of 45 (Scopus). For details, see https://researchmap.jp/SY004680_MBM?lang=en.

Immune mechanisms and oxidative stress underlying the interaction of tuberculosis and diabetes

Martin Rottenberg

Microbiology, Tumor and Cell Biology, Karolinska Instiutet, Sweden

Email: Martin.rottenberg@ki.se

Short CV

Martin Rottenberg is a Professor of Infection Immunology and studies the role of the acquired immune response in infectious diseases, i.e. how the immune system reacts to infections such as tuberculosis and parasitic diseases.

Employments

Professor, Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, 2012

Degrees and Education

Docent, Karolinska Institutet, 2000

TRX Thioredoxin redox regulator of inflammasome: Redoxisome Concept

Junji Yodoi

Kyoto University, Japan

Email: yodoi@skybue.ocn.ne.jp

Abstract

Thioredoxin (TRX) a small protein with reducing activity has TRX family members widely present from ancient organisms to humans. TRX plays various roles in intracellular signal transduction and resistance to bioistress including oxidative and chemical stress, opening a new research field of TRX-related "redox regulation". TRX has the protective effect of suppressing acute inflammation and cell death caused by oxidative stress, playing an important role in the prevention and treatment of stress-related diseases. In 2014, we proposed the concept that TRX forms a functional complex called "Redoxisome" with TRX-binding protein (TBP-2/VDUP1/TXNIP), which is involved in various pathological conditions. Oxidative stress is recognized as a critical factor influencing inflammasome activity, particularly NLRP-3, NLRP-1, NLRP-6, and NLRC-4. Recently, it has been continuously reported that TRX directly binds to the inflammasome to suppress or regulate inflammation. This research outcome has elucidated the anti-inflammatory mechanism of TRX connecting Redoxisome and Inflammasome, making it a promising target for the development of safe therapeutic drugs as an alternative to steroid preparations for respiratory inflammations, including COVID-19 infections, allergic diseases, skin hypersensitivity and psoriasis.

Key words: TRX, thioredoxin, redox, inflammation, inflammasome, redoxisome, ATL, TBP-2/TXNIP

Short CV

Junji Yodoi, M.D./Ph.D.,Prof.Em Kyoto University IVR/LiMe

1965 Tennoji High School Osaka

1971 Graduated from Kyoto University, Medical School

1971-1973 Postgraduate course of medicine, Kyoto University Hospital

1974-1975 Postgraduate course in Virus Research Institute, IVR

1975- Assistant Professor in The Institute for Immunology, Faculty of Medicine, Kyoto University

1977-1980 Research associate in Johns Hopkins University, Department of Medicine, Prof. Kimishige Ishizaka

1981- 1989 Assistant Professor The Institute for Immunology, Faculty of Medicine, Kyoto University

1989-1990 Professor in the Department of Prevention and Therapeutics, Institute for Virus Research, Kyoto University

1990-2000 Professor in the Department of Biological Responses, Institute for Virus Research, Kyoto University

2001- 2004 Human Stress Signal Research Center, BioMedical Special Research Unit, AIST at Kansai Head Joint Appointment

2003- 2008 Kyoto Univ, Translational Res Center, Thioredoxin Project, Group Leader

2003- Redox Bio Science Inc (Kyoto, Japan), Director CTO

2004- International Redox Network (IRN) , President

2010- Japan Biostress Research Promotion Alliance (JBPA), President

2010- Kyoto Univ, Prof.Em. IVR/LiMe

2011-2013 Invited Distinguished Professor in Ehwa Womans Univ. (WCU) Seoul.

2010 – Present Professor Em. Kyoto University, Chairman JBPA(Japan Biostress Research Promotion Alliance)

A systemic effects of herbal medicine on colon diseases

Mee-Hyun Lee

College of Korean Medicine, Dongshin University; Gut-Brain System Regulation Korean Medicine Research Center (GBRC), Naju, Jeonnam 58245, Korea

Email: mhyun_lee@hanmail.net

Abstract

Traditional herbal medicine has shown many pharmacological activities such as anti-inflammations, antioxidant and anticancer. Each major component targets specific counterpart and mediates various signaling processes to regulate diseases. From the ancient period, Bi-Wi imbalance has been known to cause various diseases which is reflect to the microbiome imbalance in the present. Recently, the study of gut microbiome has getting attention cause of its important role in maintaining human health by immune system modulation, gut structural regulation and dietary nutrient metabolism. When the microbiome community profiles become to imbalance, it is caused to many kinds of diseases including, and inflammatory bowel disease, depression, arthritis, diabetes, obesity, atherosclerosis, non-alcoholic fatty liver disease and cancer. In the gut microbiome regulation, traditional herbal medicine can increase the beneficial gut microbial community profiles while decreasing the harmful microbial abundance. It is metabolized into active metabolites by the action of gut microbiota, restores the microbiome balances and enhance the fermentation products of the microbiomes, thus inhibits the gut microbiota dysbiosis-derived diseases. Taken together the traditional herbal medicine can be used for prevention and therapy in a disease by regulating the targets and gut microbiota balance. Therefore, the systemic regulation by traditional herbal medicine might be a new dimensional therapeutic strategy for disease treatment

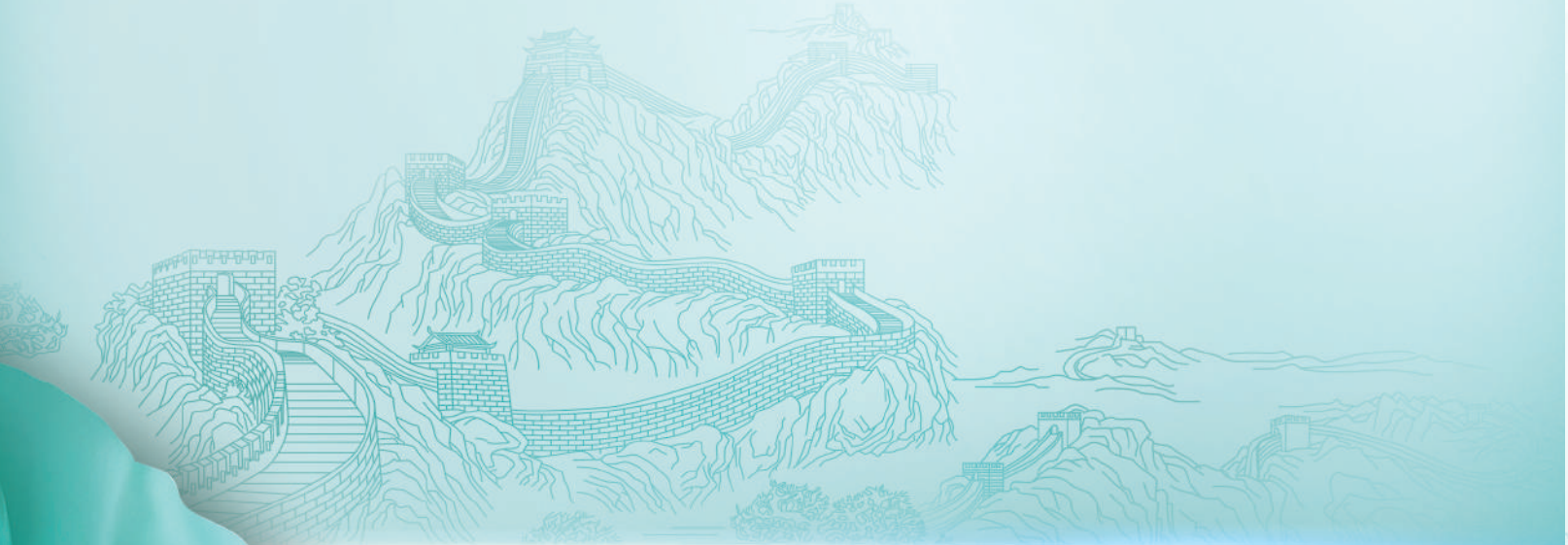
Key words: Traditional Herbal Medicine, Targeted therapy, Gut Microbiome Balance

Short CV

Professor Lee is currently an Assistant Professor at Dongshin University and the Director of the Gut-Brain System Regulation Korean Medicine Research Center (GBRC) in South Korea. She received PhD from Seoul National University, where was supervised by Professor Young-Joon Surh. She also completed postdoctoral training under Professor Zigang Dong at The Hormel Institute, University of Minnesota, USA. Additionally, she has worked at the China-US (Henan) Hormel Cancer Institute in Zhengzhou, China. Her current research interests focus on investigating novel targets and natural compounds within cancer/carcinogenesis signaling networks, and the gut microbiome. (https://scholar.google.com/citations?user=IZy6bdEAAAAJ&hl=en)

Symposium-10(S10)

Redox and environmental challenge



Chair: Libo Du(杜立波)

Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

Email: dulibo@iccas.ac.cn

Short CV

Dr. Libo Du is the associate professor of Institute of Chemisty, Chinese Academy of Sciences (CAS). He obtained his bachelor's degree from Shandong University of Technology in 2003 and M.D from Dalian University of Technology in 2006, and his Ph.D. from Institute of Chemistry, Chinese Academy of Science in 2009. Then, he joined Prof. Yang Liu's Lab as an assistant professor. In 2014, he became an associate professor of Institute of Chemistry, Chinese Academy of Science.

Dr. Du is involved in the design and synthesis of fluorescent probe that used for the monitoring the process of oxidative stress and reactive oxygen species. Furthermore, his team also focused on the nanodrug delivery system for the treatment of neurodegenerative diseases and skin disease. Recently, Dr. Du focused on the design and synthesis of peptides against skin anti-aging and anti-inflammatory.Dr. Du has published more than 80 peer-reviewed research articles and 12 authorized patents. Some patents have already been authorized for the use by the company.

Research progress and thinking of space medicine omics

Yinghui Li (李莹辉)

Astronaut Center of China; State Key Laboratory of Space Medicine, China

Email: yinghuidd@vip.sina.com

Abstract

The completion of the China Space Station marks that Chinese strategic steps in manned spaceflight have moved from short-term flights to long-term in-orbit residence. By the end of 2022, China space station has entered the application development stage. China Space Laboratory has the capability to carry out systematic and large-scale space science research, providing a unique platform for space medicine and space life science to learn about life. The goal of the mission in the field of space medical experiments is to aim at the heights of the development of space medicine, breaking through the key technologies of space medicine, improve the ability of astronauts to provide medical support, healthy life and efficient work ability, solve the main medical problems of manned space flight, and provide theoretical support and technical reserves for the future manned moon landing and deep space exploration. Focusing on the physiological effects, mechanisms and protective technologies caused by space environment, multi-system physiological changes in cardiovascular, bone and muscle metabolism, glucose and lipid metabolism, visual function, nutrient metabolism, epigenetics and other related networks were systematically carried out. This paper introduces the latest research progress of China space station. Through system analysis of foundation simulation environment, isolation environment, pre-flight and post-flight DNA methylation, transcriptome, and phenomic data in ground simulation environment, space flight DNA methylation change characteristics, super baseline recovery phenomenon and its immune system in physiological system response, combined with the international dynamic, put forward the thinking and prospect of space medical research for long-term on-orbit operation of space station.

Short CV

Yinghui Li PhD, professor, director of State Key Laboratory of Space Medicine in China Astronaut Research and Training Center. Deputy Chief Designer of Astronautic system of China's manned spaceflight project. The member of international academy of astronautics life science. Vice president of Chinese Society of Space Science and the chairman of Space Life Specialized Committee. Focus on the mechanism and application research of microgravity physiology and countermeasure, the space experiment technology of space medicine. He presided over the establishment of the state Key Laboratory of Space Medicine, which has become an important technical support platform for space station missions. She is responsible for the organization and implementation of space medicine experiment projects, and systematically conduct the occurrence and development mechanism of space medical problems, published nearly 200 SCI papers. She has made outstanding contributions to the construction of China's space medical discipline.

Gγ regulates PIP2 phosphorylation in ROS distribution to affect crop tolerant to alkaline stress

Qi Xie (谢旗)

Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, China

Email: qxie@genetics.ac.cn

Abstract

A scarcity of knowledge and breeding efforts for plant alkaline tolerance hinder the usage of alkaline-salt lands for crop production. Through genome association analysis of sorghum, a natural high-alkaline-tolerant crop, we detected a major locus, Alkaline Tolerance 1 (AT1), specifically related to alkaline-salinity sensitivity. An at1 allele with a C-terminal truncation increased sensitivity, while knockout of AT1 increased tolerance to alkalinity in sorghum, millet, rice and maize. AT1 encodes an atypical G protein γ subunit that affects the phosphorylation of aquaporins to modulate the distribution of H_2O_2. Several key factors are involved in the phosphorylation of aquaporins. These processes appear to protect plants against oxidative stress by alkali. Designing knockouts of AT1 homologues or selecting its natural nonfunctional alleles could improve crop productivity in sodic lands.

Short CV

Prof. Qi Xie, investigator of the Institute of Genetics and Developmental Biology at the Chinese Academy of Sciences. Focusing on the molecular mechanism of plant stress biology, while also working on sustainable agriculture, especially how to use saline-alkaline land for crop production.

Particulate matter and reactive oxygen species

Jin Won Hyun

Department of Biochemistry, College of Medicine and Jeju Natural Medicine Research Center, Jeju National University, Korea

Email: jinwonh@jejunu.ac.kr

Abstract

Our previous studies showed that particulate matter 2.5 (PM2.5)-derived reactive oxygen species (ROS) caused skin cell damage, cellular senescence, and inflammation. Therefore, we sought to elucidate the mechanisms of how PM2.5-derived ROS are generated. The present studies demonstrated that PM2.5-drived ROS production in human keratinocytes was mediated via the NADPH oxidase (NOXs) system and the calcium signaling pathway. PM2.5 increased the expression of NOX1, NOX4, and a calcium-sensitive NOX, dual oxidase 1 (DUOX1). PM2.5 bound to aryl hydrocarbon receptor (AhR), and this complex bound to XRE sequences of NOX1 and DUOX1 promoter regions, suggesting that AhR acted as a transcription factor of NOX1 and DUOX1. PM2.5 increased the DUOX1 transcription through epigenetic modification in terms of DNA methylation and histone modification. A link between DNA demethylase and histone methyltransferase in DUOX1 promoter elevated the expression of DUOX1 mRNA. The increase in intracellular calcium level activated DUOX1, responsible for ROS production. Our findings provide evidence for a PM2.5-mediated ROS-generating system network, in which increased expression of NOX system serves as a ROS signal through AhR and calcium activation (RS-2023-00270936). <Kang KA, et al. Environ Pollut. 2024;347:123675.>.

Key words: Particulate Matter, Reactive Oxygen Species, NADPH oxidase

Short CV

2002-present	Professor	Jeju National University School of Medicine
2023-present	Center Director	Jeju Research Center for Natural Medicine of Core Research Institute (NRF)
2017-2020	BRL Director	Basic Research Laboratory (NRF)
2012-2014	Vice-Dean	Vice-Dean of Academic Affairs in Jeju National University
2005-2014	Research Director	Jeju Regional Cancer Center, Jeju National University Hospital

TCDD-induced lysosomal SLC46A3 modulates hepatic cytosolic copper homeostasis resulting in triglyceride accumulation

Jung-Hwan Kim

Department of Pharmacology, School of Medicine, Institute of Health Sciences, Department of Convergence Medical Science, Gyeongsang National University, Jinju, 52727, Korea

Email: junghwan.kim@gnu.ac.kr

Abstract

The environmental contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) causes hepatic toxicity associated with prominent lipid accumulation and oxidative stress. Here, the authors report that the lysosomal copper transporter SLC46A3 is induced by TCDD and underlies the hepatic lipid accumulation in mice, potentially via effects on mitochondrial function. SLC46A3 was localized to the lysosome where it modulated intracellular copper levels. Forced expression of hepatic SLC46A3 resulted in decreased mitochondrial membrane potential and abnormal mitochondria morphology consistent with lower copper levels. SLC46A3 expression increased hepatic lipid accumulation similar to the known effects of TCDD exposure in mice and humans. The TCDD-induced hepatic triglyceride accumulation was significantly decreased in Slc46a3 − / − mice and was more pronounced when these mice were fed a high-fat diet, as compared to wild-type mice. These data are consistent with a model where lysosomal SLC46A3 induction by TCDD leads to cytosolic copper deficiency resulting in mitochondrial dysfunction leading to lower lipid catabolism, thus linking copper status to mitochondrial function, lipid metabolism, and TCDD-induced liver toxicity. <Kim JH et al, Nature Commun, 2021;12:290.>

Key words: slc46a3, tcdd, copper, mitochondria, fatty liver

Short CV

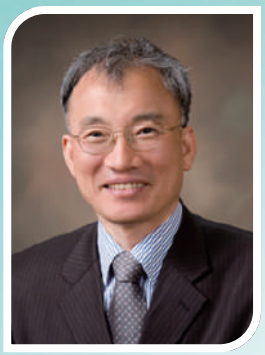
2024- present: Professor, Dept of Pharmacology, School of Medicine, Gyeongsang National. University, Republic of Korea

2018- 2024: Associate professor, Dept of Pharmacology, School of Medicine, Gyeongsang National. University, Republic of Korea

2014- 2018: Assistant professor, Dept of Pharmacology, School of Medicine, Gyeongsang. National University, Republic of Korea

2009-2014: Post-doctoral fellow in NCI/NIH, Bethesda, MD

2003- 2009: Ph.D, Pharmaceutical Science at the College of Pharmacy, Rutgers University, New. Jersey, USA



Redox history of earth, and life of organisms and foods crops

Dae Young Kwon

Institute of Food Science and Culture, # 1-1109, Yongin City, 17015, Korea.

Email: dykwon53@gmail.com

Abstract

The history of the earth is largely based on the redox potential of hydrogen and oxygen. When the earth broke away from an asteroid 4.5 billion years ago (BYA), it was in the form of a magma sea, surrounded by high-temperature and high-pressure water vapor and carbon dioxide. At 3.8 billion years old, as the high temperature fell, the water vapor became water to form an ocean without any oxygen. As the sea was formed, the cyanobacteria (photosynthetic bacteria) emerged and absorbed carbon dioxide to form limestone and oxygem in 3.0 to 3.5 BYA, resulting redox potential increased high during 2.5 to 3.0 BYA, and resulted into mass extinction of 99% of existing life at 2.4 to 2.0 BYA. Subsequent evolution of Eukaryotes by dominating the photosynthetic solar driven and oxygen-based earth system in 1 BYA. Thus plants and animal were apeared in earth in 0.5 BYA. Extinction of large animals such as dinosaurs are by asteroid collision at 65 million years ago (MYA) that allowed to mammals emerge to dominate photosynthetic and oxygen rich world to hominids 1-4 MYA and Homo sapiens 60,000 to 250,000 years ago. In order for the Earth to create a sustainable environment in the future along with climate change, we need to know about these Earth's oxido-reduction ecological systems. Similarly, humans use these redox-potential to maintain the health human body. The mission is how we can reduce oxidative stress in human biological systems. For this purpose, along with the evolution of life on the Earth, human can reduce redox potential by foods. Plants and food crops produce antioxidant materials in themselves that remove many free radicals. Individual human health also becomes a problem when the redox potential changes due to the environment, fatigue, and disease. It is important how our body does something to lower the redox potential which goes up. First of all, it is important to relax and eat for resilience of body.

Key words: Redox story of earth, cyanobacteria, photosynthetic plants, Biology, Reactive Oxygen Species.

Short CV

DYK is a fellow of the Korean Academy of Science/Technology and was professor at Hoseo Univ. He acted as President of Korea Food Research Institute, where he worked almost 35 yr. He obtained his BS at Seoul National Univ with Food Science, and he received his MS and PhD from KAIST with Biological Science. He joined Whitehead Institute, MIT, USA as a post-doctoral fellow. He is now working as President of Institute of Food Science and Culture. He is also working as Editor in Chief of J. Ethnic Foods, by Springer-Nature.

Symposium-11(S11)

Traditional Medicine Prophylaxis-Therapeutics and Redox Balance

Chair: Simon Ming-Yuen Lee (李铭源)

The Hong Kong Polytechnic University, Hongkong, China

Email: simon-my.lee@polyu.edu.hk

Short CV

Simon Ming Yuen LEE is currently Chair Professor of Biomedical Sciences in Department of Food Science and Nutrition, and State Key Laboratory of Chemical Biology and Drug Discovery, The Hong Kong Polytechnic University. Simon obtained PhD degree in biochemistry from The Chinese University of Hong Kong. His research interests lie in the discovery of drug-like agents from natural products including small molecules and biologics for use in various therapeutic areas, including brain disorder and neurodegenerative diseases. His dedication to education and research in the fields of omics, pharmacology and toxicology has leaded to over 360 scholarly articles, including Nature, Nature Genetics, Nature Communications (4×) and Science Advances. Simon is in Stanford university's list of top 2% of most-cited scientists in Pharmaceutical Science and Biology (with h-index: 65 from Scopus). Simon is a life member of Clare Hall, University of Cambridge. He has served as an editorial board member for numerous international journals including Chinese Medicine, Antioxidants, Journal of Ethnopharmacology, and Water Biology and Security.

Traditional Chinese medicine ameliorates cardiac and cerebral microvascular injury through regulating mitochondrial respiratory chain

Jing-Yan Han (韩晶岩)

Department of Integration of Chinese and Western Medicine, School of Basic Medical Sciences, Peking University, China

Email: hanjingyan@bjmu.edu.cn

Abstract

Cardiac microvascular effusion after myocardial infarction vascular recanalization and cerebral infarction vascular recanalization are both unsolved clinical problems. The method of supplementing plasma albumin and diuresis based on the theory of osmotic pressure and tissue pressure is not clinically effective. The clinical effect of traditional Chinese medicine in the treatment of cardiovascular and cerebrovascular exudation is obvious, but the mechanism of action of qi replenishment and intake is not clear.

The team of the presenters used a rat cardiac microvascular exudation model established by cardiac ischemia and reperfusion to confirm that Qishen Yiqi Dripping Pill, a compound Chinese medicine that replenishes Qi and invigorates blood, can inhibit cardiac microvascular exudation in rats caused by ischemia and reperfusion, which is related to improving the energy metabolism of vascular endothelial cells and inhibiting the opening of vascular endothelial cell gap links.

The reporter's team also used a mouse cerebral microvascular exudation model established by tPA thrombolysis after middle cerebral artery cerebral infarction to confirm that Qi Replenishing and Activating Blood Compound Chinese Medicine Qishen Yiqi Dripping Pill can inhibit cerebral microvascular exudation and hemorrhage in mice after tPA thrombolysis after middle cerebral artery cerebral infarction, which is related to improving the mitochondrial respiratory chain of vascular endothelial cells, improving energy metabolism, and inhibiting the opening of vascular endothelial cell gap links. , inhibition of vascular basement membrane injury.

In this report, we will introduce the mechanism of action of Qi Replenishing and Invigorating Blood Compound Chinese Medicine to improve the mitochondrial respiratory chain and improve the exudation of cardiovascular and cerebral microvessels.

Short CV

Professor Jing-Yan Han graduated from Liaoning University of traditional Chinese medicine in 1982. He obtained his doctor degree in the department of internal medicine at the Keio University School of Medicine in Japan in 2002. In 2004, he became the Director of the Tasly microcirculation research center at the Peking University Health Science Center. In 2008, he was appointed as the Chair and Professor of the department of integration of Chinese and Western medicine at the School of Basic Medical Sciences of Peking University. In 2009, he served as a visiting professor in the department of internal medicine at the Keio University School of Medicine. In 2010, he became the chair of the department of integration of Chinese and Western medicine at the Peking University Health Science Center. In 2019, he was appointed as the Dean of Academy of Integration of Chinese and Western Medicine, Peking University Health Science Center.

Niuhuang Qingxin Wan ameliorates depressive-like behaviors and improves hippocampal neurogenesis through modulating TrkB/ERK/CREB signaling pathway in chronic restraint stress or corticosterone challenge mice

Jiangang Shen

School of Chinese Medicine, University of Hong Kong, 3 Sassoon Road, Hong Kong, Hong Kong SAR, China.

E-mail: shenjg@hku.hk

Introduction: Chronic stress-associated hormonal imbalance impairs hippocampal neurogenesis, contributing to depressive and anxiety behaviors. Targeting neurogenesis is thus a promising antidepressant therapeutic strategy. Niuhuang Qingxin Wan (NHQXW) is an herbal formula for mental disorders in Traditional Chinese Medicine (TCM) practice, but its anti-depressant efficacies and mechanisms remain unverified.

Methods: In the present study, we tested the hypothesis that NHQXW could ameliorate depressive-like behaviors and improve hippocampal neurogenesis by modulating the TrkB/ERK/CREB signaling pathway by utilizing two depression mouse models including a chronic restraint stress (CRS) mouse model and a chronic corticosterone (CORT) stress (CCS) induced mouse model. The depression-like mouse models were orally treated with NHQXW whereas fluoxetine was used as the positive control group. We evaluated the effects of NHQXW on depressive- and anxiety-like behaviors and determined the effects of NHQXW on inducing hippocampal neurogenesis.

Results: NHQXW treatment significantly ameliorated depressive-like behaviors in those chronic stress mouse models. NHQXW significantly improved hippocampal neurogenesis in the CRS mice and CCS mice. The potential neurogenic mechanism of NHQXW was identified by regulating the expression levels of BDNF, TrkB, p-ERK (T202/T204), p-MEK1/2 (S217/221), and p-CREB (S133) in the hippocampus area of the CCS mice. NHQXW revealed its antidepressant and neurogenic effects that were similar to fluoxetine. Moreover, NHQXW treatment revealed long-term effects on preventing withdrawal-associated rebound symptoms in the CCS mice. Furthermore, in a bioactivity-guided quality control study, liquiritin was identified as one of the bioactive compounds of NHQXW with the bioactivities of neurogenesis-promoting effects.

Conclusion: NHQXW could be a promising TCM formula to attenuate depressive- and anxiety-like behaviors against chronic stress and depression. The underlying anti-depressant mechanisms could be correlated with its neurogenic activities by stimulating the TrkB/ERK/CREB signaling pathway.

Qiliqiangxin in the treatment of heart failure with reduced ejection fraction ------ research progress

Xinli Li (李新立)

First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, China

Email: xinli3267@yeah.net

Abstract

The latest findings from the QUEST study were published in Nature Medicine. This study evaluated the efficacy and safety of Qiliqiangxin capsules (QLQX), a traditional Chinese medicine, in treating heart failure with reduced ejection fraction (HFrEF). The results marked a significant achievement, highlighting the role of Traditional Chinese Medicine (TCM) in global cardiovascular treatment.

The QUEST study, a large-scale, multicenter, randomized controlled trial involving 3,110 HFrEF patients across 133 clinical centers, demonstrated that adding QLQX to standard treatments reduced major adverse cardiovascular events by 22%, heart failure hospitalizations by 24%, and cardiovascular deaths by 17%. Importantly, QLQX did not significantly increase adverse events, confirming its safety profile.

The systemic mechanisms suggest that QLQX may work by attenuating oxidative stress and modulating the PPARγ/PGC-1α signaling pathway. This groundbreaking research offers a promising future for integrating TCM with modern medical practices in heart failure treatment.

The study not only underscores the clinical value of QLQX but also sets a precedent for the internationalization and standardization of TCM, providing a pathway for future innovations in global healthcare.

Key words: Qiliqiangxin, Heart failure, Traditional Medicine, PPARγ/PGC-1α

Short CV

Prof. Xinli Li, Chief Cardiologist, Postgraduate & Doctorate Supervisor from State Key Laboratory for Innovation and Transformation of Luobing Theory, the First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

Chinese special contribution expert of the state council, and Chief cardiologist and second-level professor of the First Affiliated Hospital of Nanjing Medical University.

Academic appointment in various academic groups including: Vice President of the Cardiovascular Branch of the Chinese Society of Gerontology, Vice Chairman of the Heart Failure Group of the Cardiovascular Branch of the Chinese Medical Doctor Association, Vice Chairman of the Hypertension Group of the Chinese Society of Cardiovascular Diseases, Vice Chairman of the Collateral Disease Branch of the Chinese Society of Chinese Medicine, Vice Chairman of the Precision Medicine Branch of the Chinese Society of Thoracic Cardiovascular Anesthesiology, etc.

Dedicated in the basic and clinical research on cardiology for decades; As the corresponding author, published more than 300 articles in various esteemed journal (Nature Medicine, JACC, Circulation, etc.); Supervised for over 100 post-graduate and doctorate students.

Cardiac stress resistance regulated by sulfur metabolism

Motohiro Nishida

Graduate School of Pharmaceutical Sciences, Kysuhu University, Japan

Email: nishida@phar.kyushu-u.ac.jp

Abstract

Sulfur-based redox signaling has long been attracted attention as critical mechanisms underlying the development of cardiac diseases and resultant heart failure. Especially, post-translational modifications of cysteine (Cys) thiols in proteins mediate oxidative stress-dependent cardiac remodeling including myocardial hypertrophy, senescence, and interstitial fibrosis. However, we recently revealed the existence of Cys persulfides and Cys polysulfides in cells and tissues, and these catenated sulfur molecules (supersulfide) substantially contribute to redox signaling and energy metabolism by exerting unique redox dynamics. We have established simple evaluation methods that can detect polysulfides in proteins and inorganic polysulfides in cells. We found that polysulfides in healthy hearts are dramatically catabolized by exposure to ischemic/hypoxic and environmental electrophilic stress, leading to vulnerability of the heart to mechanical load. Accumulation of hydrogen sulfide, a nucleophilic catabolite of persulfides/polysulfides, is well associated with myocardial remodeling, and perturbation of polysulfide catabolism can improve myocardial remodeling and dysfunctions after myocardial infarction in mice. These results suggest that prevention of supersulfide catabolism during ischemic/hypoxic stress becomes a new therapeutic strategy for the treatment of chronic heart failure.

Key words: Sulfur, heart, robustness, redox signaling, metabolism

Short CV

1996-2001 Ph. D., Graduate School of Pharmaceutical Sciences, University of Tokyo, Japan

2001.4-2001.5 JSPS Research Fellow, University of Tokyo, Japan

2001.5-2003.9 Assistant Professor, Okazaki Institute for Integrative Bioscience, Japan

2003.10-2006.7 Lecturer, Graduate School of Pharmaceutical Sciences, Kyushu University, Japan

2006.8-2013.7 Associate Professor, Graduate School of Pharmaceutical Sciences, Kyushu University, Japan

2013.8- Professor, National Institute for Physiological Sciences (NIPS) & Exploratory Research Center on Life and Living Systems (ExCELLS), National Institutes of Natural Sciences, Aichi, Japan

2013.10-2017.3 Research Fellow, JST, PRESTO, Japan

2020.4- Professor (80%), Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan

Cross Appointment Professor (20%), NIPS&ExCELLS, NINS, Japan

The role of oxidative stress and antioxidants in liver disease therapy

Yibin Feng（冯奕斌）
The University of Hong Kong, China
Email: yfeng@hku.hk

Abstract

Over 10% of the world population is affected by various kinds of liver diseases. Liver diseases including acute virus hepatitis, chronic virus hepatitis, alcoholic and non-alcoholic fatty liver, liver fibrosis, cirrhosis and liver cancer etc., are serious health-threaten problems worldwide, especially in Asian region. In addition to various etiologic facts, base of liver diseases are inflammatory diseases and associate with oxidative stress. In fact, oxidative stress plays an important role in chain of liver diseases. Various pathological factors damaged liver tissues by increase reactive oxygen (ROS), nitrogen species (RNS) and peroxidation of lipids, DNA, and proteins. ROS affects fibrogenesis via increasing platelet-derived growth factor and ROS/RNS provokes hepatic stellate cells, which are presented by the enhanced production of extracellular matrix and accelerated proliferation, and most hepatocellular carcinomas occur in fibrotic and cirrhotic livers. There are complicated cross-talk among pathological factors, inflammatory, free radicals and immune responses. Finding network and mechanisms linking these relationship and process will play a major role in pathogenesis of liver diseases. It is still far to reach it, but targeting any specific etiological or pathological factor should be one of reasonable therapeutic strategy in liver diseases. For this purpose, antioxidative therapy maybe become a basic treatment for various liver diseases. Based on literature review and our original studies, I will review oxidative stress and relationship among other etiological and pathological factors in liver diseases, and then explore possibility of antioxidative therapy for liver diseases.

Key words: inflammatory, oxidative stress, antioxidants, liver disease, therapy

Short CV

Dr. Feng Yibin is currently a professor and Director of the School of Chinese Medicine, University of Hong Kong. Mainly focus on integrative Chinese and Western medicine in the prevention and treatment of cancer and metabolic diseases. He has published more than 600 various kind of publications, among which over 200 SCI papers in reputable international journals. According to InCites Essential Science Indicators (ESI), Dr. Feng has been listed as one of the top 1% of scholars in the world at the University of Hong Kong for 8 consecutive years, and is also listed as one of top 2% Scientists Worldwide by Stanford University. He contributes to academic community as the chairperson at the international conferences and has given keynote, plenary/ invited speeches over 200 around the world. He is the editor of several international journals in his field and reviewer for lots of international journals.

Symposium-12(S12)

Natural products and nutrition in anti-aging and health management

Chair: Bo Zhou (周波)

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, China

Email: bozhou@lzu.edu.cn

Short CV

Bo Zhou obtained his BS degree in Chemistry from Gannan Normal University in China in 1993, followed by MS and PhD degrees in Organic Chemistry from Lanzhou University in 1997 and 2000, respectively. After completing his postdoctoral work at Life Science College and State Key Laboratory of Applied Organic Chemistry, Lanzhou University, he joined the college of chemistry and chemical engineering at Lanzhou University. In 2004, he was promoted to the position of professor. He received support from the Program for New Century Excellent Talents in University in 2006, and selected as a member of the Executive Committee for SFRBM of China in 2018.

His research interests primarily focus on developing pro-oxidative anticancer agents inspired by natural products to target abnormal redox homeostasis within cancer cells. Additionally, he is involved in designing fluorescent probes for monitoring intracellular redox-active molecules. He has published over 120 scientific papers across various international journals including J. Am. Chem. Soc., Anal. Chem., Free Radic. Biol. Med., Sens. Actuators B Chem., Chem. Eur. J., Antioxid. Redox Signaling, J. Org. Chem., with an H-index of 42.

Chair: Ae-Son Om

Hanyang University, Korea

Email: aesonom@hanyang.ac.kr

Short CV

EDUCATIONAL BACKGROUND

1996.09 - 1999.06 Michigan State University Department of Food Science & Human Nutrition Ph.D.
1993.08 - 1996.08 University of Oklahoma Department of Anatomy & Cell Biology Ph.D.
1988.03 - 1991.08 Hanyang University Department of Food and Nutrition Ph.D.
1983.09 - 1985.08 Hanyang University Department of Food and Nutrition M.S.
1979.03 - 1983.03 Hanyang University Department of Food and Nutrition B.A.

AWARDS AND HONORS

2016.12 Appreciation Award from Army Chief of Staff, Ministry of National Defense
2013.05 12th Food Safety Day Diligence Award, Ministry of Food and Drug Safety
2013.04 Commendation Award from Minister, Ministry of Health & Welfare

POSITIONS HELD TO DATE

2023.02 - Now Member of the Agriculture, Fisheries and Food Subcommittee of the Presidential Committee on Agriculture
2021.04 - Now Non-executive Director of Korea Food Safety Management Certification Institute (HACCP)
2021.03 - Now Chairman of the Agricultural and Fishery Products Hygiene and Safety Ingredients Division of the Ministry of Agriculture, Food and Rural Affairs
2021.01 - 2023.01 Non-executive Director of Korea National Cluster
2021.01 - 2021.12 Vice President, Korean Society of Food Science and Technology
2019.01 - 2021.01 Prime Minister's Office Food Safety Policy Committee
2019 - 2021 Vice Chairman of the Health Functional Food Advertisement Review Committee
2014.06 - 2022.12 Chief of Center for Children's Foodservice Management
2014.02 - Now President in the 11th Hanyang University HACCP education and training institution appointed by the Ministry of Food and Drug Safety
2008.01 - 2013.01 President in The Korean Society of Food Service Sanitation
2006 - 2009 Member of the Health Functional Food Advertisement Review Committee

PUBLICATIONS

Food Hygiene (Revised Edition) (Text Book), 2022
The impact of COVID-19 on older persons in Republic of Korea, 2020
Life Planning series 2, 2016
54 Korean Dietary Ingredients Against Cancer, 2013
Science of A Cup of Milk, 2010
Food Microbiology (Text Book), 2009
Current Food Sanitation (Text Book), 2005

International academic journal activities

2022.07 - 2023.03 Editor of Journal of Fungi
2021.03 - 2022.06 Editor of Toxins

RESEARCH PROJECTS

■ Hanyang University Food Tech Department Operation

2020 - Now Department Head, Department of Food Tech Functional Food, Hanyang University: Education for employees and students of about 40 small and medium-sized companies)

■ Industrial technical guidance/consultation (HACCP, expiration date setting experiment, etc.)

2022 - Now NST Bio, Our Bio Consulting

2019 - 2020 Medipresso, Shinan Tourism Co., Ltd., Doojin Food, Vitamin Tree HACCPConsulting (HACCP Certification Success)

2018 - 2018 Mac Bakery Co., Ltd., Hotel Rivera HACCP Consulting (Successful HACCP Certification)

2017 - 2018 Gwangjin Food Co., Ltd., International Comprehensive Consulting, Ubok-dong, Jinheung Agricultural Products, Hanul Comprehensive Food, Hana Architects & Engineers Co., Ltd. HACCP Consulting (HACCP Certification Success)

■ Military food service consulting and research and development

Combat Rations Research

2017 - 2022: L-type distribution period setting and ILS test

2016 - 2016: Combat ration utilization and stockpiling feasibility study of outdoor food

2015 - 2016: Preliminary research service for development of L-type personal combat rations

■ Hygiene and safety education (hygiene education and consulting for students, civil servants, companies, group meals, military meals, food processing companies, etc.)

2018 - 2018 Seoul Metropolitan City School Health Promotion Center Education: Specialized training for school meal hygiene and safety inspection personnel

2017 - 2017 Seoul Metropolitan Office of Education: Specialized training for school meal hygiene and safety inspection personnel

LIST OF JOURNALS AND PAPERS (10 Representative Papers)

1. Hong, J. Y., Kim, Y. M., Shin, M. H., Lee, Y. H., Om, A. S., & Kim, M. K. (2022). Development and validation of dietary atherogenic index using common carotid artery-intima-media thickness: A food frequency questionnaire-based longitudinal study in Korean adults. Nutrition Research, 104, 55-65.

2. Wei, X., Du, M., Hong, S. Y., & Om, A. S. (2022). Degradation of Patulin in Pear Juice and Apple Juice by Ascorbic Acid and the Combination of Ascorbic Acid and Ferrous Iron. Toxins, 14(11), 737.

3. Choo, M. J., Hong, S. Y., Chung, S. H., & Om, A. S. (2021). Removal of aflatoxin B1 by edible mushroom-forming fungi and its mechanism. Toxins, 13(9), 668.

4. Sun, X., Xuan, X., Ji, L., Chen, S., Liu, J., Zhao, S., ... & Om, A. S. (2021). A novel continuous hydrodynamic cavitation technology for the inactivation of pathogens in milk. Ultrasonics sonochemistry, 71, 105382.

5. Choi, Y., Kim, D. S., Lee, M. C., Park, S., Lee, J. W., & Om, A. S. (2021). Effects of bacillus subtilis-fermented white sword bean extract on adipogenesis and lipolysis of 3T3-L1 adipocytes. Foods, 10(6), 1423.

6. Lee, M. C., Puthumana, J., Lee, S. H., Kang, H. M., Park, J. C., Jeong, C. B., ... & Lee, J. S. (2016). BDE-47 induces oxidative stress, activates MAPK signaling pathway, and elevates de novo lipogenesis in the copepod Paracyclopina nana. Aquatic Toxicology, 181, 104-112.

7. Lee, M. C., Han, J., Lee, S. H., Kim, D. H., Kang, H. M., Won, E. J., ... & Lee, J. S. (2016). A brominated flame retardant 2, 2 □ , 4, 4 □ tetrabrominated diphenyl ether (BDE-47) leads to lipogenesis in the copepod Tigriopus japonicus. Aquatic toxicology, 178, 19-26.

8. Om, A. S., Song, Y. N., Noh, G., Kim, H., & Choe, J. (2016). Nutrition composition and single, 14-day and 13-week repeated oral dose toxicity studies of the leaves and stems of Rubus coreanus Miquel. Molecules, 21(1), 65.

9. Kim, I., Kim, H. R., Kim, J. H., & Om, A. S. (2013). Beneficial effects of Allium sativum L. stem extract on lipid metabolism and antioxidant status in obese mice fed a high-fat diet. Journal of the Science of Food and Agriculture, 93(11), 2749-2757.

10. Om, A. S., & Shim, J. Y. (2007). Effect of daidzein in rats on cadmium excretion. Bulletin of environmental contamination and toxicology, 78, 485-488.

Research on space biological rhythm intervention strategies based on redox regulation

Lina Qu (曲丽娜)

State Key Laboratory of Space Medicine, China Astronaut Research and Training Center, China

Email: linaqu@263.net

Abstract

During space exploration, astronauts expose consistently or intermittently to various environmental factors, including weightlessness, radiation, noise, isolation and confinement. All these factors combine to exert stress responses on many aspects of physiological systems, eliciting influence on astronaut's health. Long-term spaceflight is known to induce disruption in circadian rhythm and cognitive disturbance, but the underlying molecular mechanism remain unclear. More evidences have shown change of redox status and elicited increased oxidative stress during space flight.

Circadian rhythm is a widespread physiological phenomenon which exists in almost all of the life forms and comprises a system of interconnected transcriptional and translational feedback loops. It has been known that the oxidative stress involved in many diseases and injuries like aging, Alzheimer disease, diabetes and cancers. There have been growing literatures about the biological rhythm disorder caused by oxidative stress, but little is known about the effect of oxidants on circadian rhythm intervention and the potential mechanism.

In our research, we have found that H_2O_2 could modulate the circadian rhythm of Bmal1 via RORα, REV-ERBα (NR1D1) and REV-ERBβ (NR1D2). N-Acetyl cysteine could reverse the H_2O_2 induced up-regulation of CLOCK and BMAL1, period shorten and amplitude elevation of Bmal1-luciferase, providing evidences that the non-transcriptional oscillation may interplay with the transcriptional/translational feedback loops. In simulated microgravity and isolation condition, transcription factor Nrf2 might regulate biological rhythm by regulating the expression of the CLOCK, and mitophagy exerts circadian control by regulating NR1D1 degradation. In space simulated environment, rats were treated with urolithin A, a mitophagy activator derived from pomegranate nuts and berries, reversed the disruption of central body temperature, heart rate and activity rhythms by increasing mitophagy to decay NR1D1 and improving mitochondrial function. The activation of mitophagy holds great promise as a therapeutic strategy for long-term spaceflight as well as diseases with circadian disruption.

Key words: Space flight, Biological rhythm, Redox regulation, Oxidative stress

Short CV

Professor, State Key Laboratory of Space Medicine, China Astronaut Research and Training Center; Major in research of space medicine fundamental and application, especially on redox regulation in space medicine.

Phosphatidylethanolamine alleviates OX-LDL-induced macrophage inflammation by upregulating autophagy and inhibiting NLRP1 inflammasome activation

Qinghui Ai (艾庆辉)

Key Laboratory of Aquaculture Nutrition and Feed (Ministry of Agriculture and Rural Affairs), Ocean University of China, China

Email: qhai@ouc.edu.cn

Abstract

Oxidized low-density lipoprotein (OX-LDL)-induced inflammation and autophagy dysregulation are important events in the progression of atherosclerosis. Phosphatidylethanolamine (PE), a multifunctional phospholipid that is enriched in cells, has been proven to be directly involved in autophagy which is closely associated with inflammation. However, whether PE can influence OX-LDL-induced autophagy dysregulation and inflammation has not been reported. In the present study, we revealed that OX-LDL significantly induced macrophage inflammation through the CD36-NLRP1-caspase-1 signaling pathway in fish. Meanwhile, cellular PE levels were significantly decreased in response to OX-LDL induction. Based on the relationship between PE and autophagy, we then examined the effect of PE supplementation on OX-LDL-mediated autophagy impairment and inflammation induction in macrophages. As expected, exogenous PE restored impaired autophagy and alleviated inflammation in OX-LDL-stimulated cells. Notably, autophagy inhibitors reversed the inhibitory effect of PE on OX-LDL-induced maturation of IL-1β, indicating that the regulation of PE on OX-LDL-induced inflammation is dependent on autophagy. Furthermore, the positive effect of PE on OX-LDL-induced inflammation was relatively conserved in mouse and fish macrophages. In conclusion, we elucidated the role of the CD36-NLRP1-caspase-1 signaling pathway in OX-LDL-induced inflammation in fish and revealed for the first time that altering PE abundance in OX-LDL-treated cells could alleviate inflammasome-mediated inflammation by inducing autophagy. Given the relationship between OX-LDL-induced inflammation and atherosclerosis, this study prompts that the use of PE-rich foods promises to be a new strategy for atherosclerosis treatment in vertebrates.

Key words: Oxidized low-density lipoprotein, Macrophages, NLRP1 inflammasomes, IL-1β, Phosphatidylethanolamine, Autophagy

Short CV

Professor of Ocean University of China (OUC), Dean of Fisheries College, OUC. Distinguished professor of Changjiang Scholars, the recipient of the National Outstanding Youth Science Foundation of China and a national young and middle-aged science and technology innovation leader. He is mainly engaged in the research of lipid nutrition and immune metabolism in fish, and has explored the lipid metabolism, inflammatory response and its regulatory mechanism in marine fish, and proposed corresponding mitigation strategies, which has promoted the development of aquatic animal nutrition and the healthy and sustainable development of aquatic feed industry. The research results have been published in Progress in Lipid Research, Reviews in Aquaculture, Cell Death and Disease, Free Radical Biology and Medicine, iScience, FASEB and other journals, with more than 200 papers. Meanwhile, he has also obtained 28 national and international patents.

Translation of bilirubin's redox potential to preventative and therapeutic medicine – use of models, and the development of therapies

Andrew Bulmer

Griffith University, Australia

Email: a.bulmer@griffith.edu.au

Abstract

Bilirubin's antioxidant effects are well established, and protects against various pathologies underpinned by oxidative stress. Despite this, understanding whether bilirubin can prevent and/or treat pathologies that induce oxidative stress in humans remains unknown. A number of animal models are available to test these effects, however, very few induce physiologically relevant bilirubin concentrations, questioning the relevance of findings. Interestingly, the unique human model of Gilbert's syndrome provides a relevant model to test bilirubin's potential protective effects, however, can only provide correlative data. Therefore, our group developed a titratable inducible hyperbilirubinaemic mouse model, to test the potential beneficial effects of bilirubin, addressing issues relating to bilirubin concentration and providing a means to test preventative and therapeutic effects. This presentation will also discuss potential therapeutic strategies in humans and identify conditions that bilirubin is most likely protective against, based upon currently published literature. It is hoped that this presentation will stimulate research in the area, particularly concerning the development of therapeutics that can increase bilirubin, for prevention and treatment of age related pathologies.

Key words: Bilirubin, Haem Oxygenase, UGT1A1, cardiovascular disease, diabetes, animal model, Gilbert's Syndrome

Short CV

Professor Bulmer is a research intensive academic within the School of Pharmacy and Medical Sciences at Griffith University on the Gold Coast, Australia. Dr Bulmer has more than 20 years of experience in biochemistry, haematology and cardiovascular imaging, including their use in a variety of in vitro, *in vivo* small animal, pre-clinical human and human clinical trial research settings. Using this experience, his Experimental Laboratory Science (XLabS) research group aims to better understand and prevent the effects of vascular injury within the arterial and venous circulation. Dr Bulmer's research has two foci, the first includes demonstrating the protective effects of haem catabolism and bilirubin formation within inflammatory pathology, particularly in atherosclerosis. Secondly, his group aims to reduce vasculitis and thrombotic events in patients enduring invasive vascular access devices/procedures with the AVATAR group (https://www.avatargroup.org.au/).

A catechol isoquinoline salsolinol induces apoptosis of human liver cancer cells by regulating the STAT1/3 Signaling

Hye-Kyung Na

Basic Science Research Institute, Sungshin Women's University, Korea

Email: nhk1228@sungshin.ac.kr

Abstract

Liver cancer is one of the most common malignancies and a leading cause of death worldwide. However, it is still very difficult to treat and prevent liver cancer. A catechol tetrahydroisoquinoline, salsolinol (SAL) is present in our daily diets, such as mushrooms, bananas, etc. It is also endogenously generated by the condensation of dopamine with acetaldehyde. In the present study, we found that SAL inhibited the growth and colony forming ability of human hepatic carcinoma SK-Hep1 cells. The phosphorylation at Tyr 705 of signal transducer and activator of transcription factor 3 (STAT3) and its dimerization, nuclear translocation, and transcriptional activity were inhibited by SAL. The expression of cyclin D1, the major target proteins of STAT3, was suppressed, whereas the expression of cell cycle regulator p21 and its upstream regulator p53 was enhanced by SAL. p53 regulates expression of genes involved in apoptosis. SAL induced intrinsic apoptotic signaling by enhancing Bax expression and proteolytic cleavage of caspase-9/3/7 and PARP. The proportions of cell population in the subG0/G1 fraction and TUNEL positive apoptotic cells were increased by SAL. SAL inhibited the mitochondrial STAT3 phosphorylation (Ser727) and induced disruption of mitochondria membrane potential, which led to the downregulation of cytochrome c in the mitochondria fraction. A general antioxidant N-acetyl cysteine (NAC) attenuated suppression of STAT3 at Tyr and Ser residues and blocked the phosphorylation of STAT1 (Tyr 701) and cell death as well as generation of reactive oxygen species induced by SAL. Moreover, SAL inhibited direct interaction between Annexin A2 and STAT3 (Ser727), thereby suppressing phosphorylation of STAT3 (Ser727). Furthermore, intraperitoneal injection of SAL significantly delayed the growth of tumor and reduced the tumor volume in a SK-Hep1 xenograft mouse model. Taken together, SAL regulates STAT1/3 signaling, thereby inducing apoptosis in SK-Hep1 cells, which may account for its anti-carcinogenic activity in liver cancer.

Key words: Salsolinol, STAT3, STAT1, Liver cancer, Cell Death

Short CV

Hye-Kyung Na is a professor of Food Science & Biotechnology, College of Knowledge-Based Services Engineering, Sungshin Women's University, Seoul, South Korea. Prof. Na's research focuses on molecular mechanisms underlying anti-oxidant, anti-inflammatory, and anti-carcinogenic activities of dietary and medicinal phytochemicals targeting STATs and 15-hydroxyprostaglandin dehydrogenase in liver, breast, and colon carcinogenesis models.

From target identification to early-stage therapeutic discovery: leveraging *in vivo* preclinical models

Yun-Sil Lee

College of Pharmacy and Graduate School of Pharmaceutical Science, Ewha Womans University, Seoul, Korea

Email: yslee0425@ewha.ac.kr

Abstract

Idiopathic pulmonary fibrosis (IPF) is an interstitial lung disease of unknown cause, marked by irreversible damage to lung structure and function. Currently, the therapeutic drugs available for pulmonary fibrosis include pirfenidone and nintedanib. However, these drugs are not economically viable and require relatively high doses, which lead to significant side effects. Thus, it is necessary to discover novel targets and develop therapeutics based on these targets for IPF treatment. To identify the molecular signatures of lung fibrosis, we investigated the fibrotic process in irradiated areas of mouse fibrotic lung tissues, identifying GTSE1 and autophagy-senescence axis as targets for lung fibrosis. We have also developed novel therapeutics targeting these new discoveries, and we would like to take the opportunity to introduce these findings.

Key words: Idiopathic pulmonary fibrosis; Novel targets; Gtse1; Autophagy; Senescence

Short CV

Dr. Yun-Sil Lee is a full professor at the Graduate School of Pharmaceutical Sciences at Ewha Womans University. She earned her B.S., M.S., and Ph.D. degrees in the College of Pharmacy at Ewha Womans University. Following her academic journey, she pursued postdoctoral research at the National Cancer Institute (NCI) in the USA. For nearly two decades, she worked as a Principal Scientist at the Korea Institute of Radiological and Medical Sciences. Her research primarily revolves around the development of radiation protectors or sensitizers. More recently, her research interests have shifted towards the development of inhibitors for pulmonary fibrosis. Professor Lee's extensive research contributions are reflected in her publication record, with over 200 SCI(E) papers. Her expertise has also earned her invitations to international symposia as an invited speaker.

Symposium-YIO-4 (Y-4)

"New approach for precision redox research
Intelligence materials for precision redox intervention"

Chair: Xianquan Zhan (詹显全)

Cancer Hospital and Institute, Shandong First Medical University, China
Email: yjzhan2011@gmail.com

Short CV

Prof. Dr. Xianquan Zhan received his MD, PhD training in preventive medicine at West China University of Medical Sciences during 1989–1999. He received his post-doctoral training in oncology and cancer proteomics at Central South University and University of Tennessee Health Science Center (UTHSC). He worked in UTHSC and Cleveland Clinic in United States during 2001–2012, and achieved the rank of Associate Professor at UTHSC. In 2012, he moved to Xiangya Hospital, Central South University as a Professor, and Advisors of MS/PhD graduate students and postdoctoral fellows. In 2020, he moved to Shandong First Medical University, where he is a Professor, Principal Investigator (PI), and advisors of MS/PhD graduate students and postdoctoral fellows at Medical Science and Technology Center. He is also the Fellow of Royal Society of Medicine, Fellow of World Academy of Productivity Science, Fellow of EPMA, European EPMA National Representative, Full member of ASCO, AAAS member, Shandong Province Taishan Scholar Distinguished Expert, Leader of medical disciplines in Hunan Province, Hunan Xiaoxiang Friendship Award, Hunan Provincial International Science and Technology Cooperation Award, Distinguished Professor of Hunan Provincial Hundred Talents Program, Jinan City class A high-level talents, Editor-In-Chief of IJCDT, Associate Editors of EPMA Journal, BMC Medical Genomics, and Frontiers in Endocrinology, and Guest Editors of Frontiers in Endocrinology, and Mass Spectrometry Reviews. He has published 180 articles, 10 academic books, 30 book chapters, and 3 international patents in the field of clinical proteomics and biomarkers, H-index 37. As the Guest Editor, he edited 18 special issues in SCI journals such as Mass Spectrometry Reviews, Frontiers in Endocrinology, EPMA Journal, Oxidate Medicine Cellular Longevity, and Med One. His main research interest focuses on the studies of cancer proteomics and proteoformics, multiomics and biomarkers, and the use of modern omics techniques and systems biology for predictive, preventive, and personalized medicine (PPPM; 3P medicine) and precision medicine (PM) in cancer.

Chemical proteomics reveals mechanisms of bacterial response to ROS mediated by antibiotics

Ling Fu (付玲)

National Center for Protein Sciences, Beijing, China

Email: flsmt@163.com

Abstract

Increasing bacterial resistance has become a major threat to human health, and a more comprehensive and in-depth understanding of the mechanisms of antibiotic sterilization can help us better address the problem of bacterial resistance. A variety of antibiotics have been proposed to cause bacterial death, in part by increasing the steady-state levels of reactive oxygen species (ROS) in bacteria. However, it remains unclear which proteins the ROS modify and their roles in antibiotic susceptibility/ resistance. To answer this question, we present a comprehensive, quantitative, and site-specific profile of E.coli cysteinome after 8 antibiotics treatment. Our data revealed antibiotic-mediated ROS targets modulate redox-sensitive events in nucleotide binding, cellular amino acid biosynthetic process, metabolic process, oxidative stress response, and etc. We also demonstrated that the tRNA-specific 2-thiouridylase MNMA_C102, the regulatory factor NEMR_C116, and TyrR_C337 are redox-regulated by antibiotic-mediated ROS, and that redox form shifts at these sites further affect enzyme activity, dimer formation, gene expression, etc., and ultimately the strain's susceptibility to antibiotics. Taken together, this study provides a molecular basis for understanding the relationship between antibiotic-mediated ROS targets and bacterial resistance, and offers a new perspective for finding new ways to enhance the bactericidal effect of existing antibiotics and developing novel antibiotics.

Key words: Antibiotic resistance, Reactive oxygen species, Cysteinome

Short CV

I joined Jing Yang's lab at the National Center for Protein Sciences • Beijing in 2015. Since then, I have been working on mapping protein S-sulfenylation (-SOH), S-sulfinylation (-SO2H) and S-Sulfhydration (-SSH) in various model organisms using state-of-the-art chemoproteomic technology. My interests mainly focus on redox proteomics to answer fundamental questions from a REDOX perspective, such as 1) Mechanism of antibiotic resistance in pathogenic bacteria; 2) Adaptation mechanism of microorganisms to extreme environments. I have published 10 research papers as the first/Co-first or co-corresponding authors in Nat Chem Biol, Nat Plants, Nat Commun, Nat Protoc, Antioxid Redox Signal and so on. Of these, 4 papers have been featured by Nature Research Journals in News & Views or Research Highlights.

Molecule-guided precise identification and intervention of senescence

Yuan Guo (郭媛)

Northwest University, China

Email: guoyuan@nwu.edu.cn

Abstract

Cellular senescence is believed to be a driver of aging. Guo's group designed and synthesized small-molecule based fluorescent probes with high spatiotemporal resolution to track senescence precisely, and developed prodrugs that destroys senescent cells by integrating multiple technologies that combine biomarker guidance with a fluorescence tag, target-site anchoring and photodynamic therapy. As such, the group created strategies for monitoring and specifically eliminating senescent cells to regulate aging. As such, they achieved: 1) the innovations in senescence/aging "tracing" approaches involving the species-specific identification of senescent-associated protein1, the two-dimensional senescence identification associated with senescent microenvironmen and the dynamic identification of aging of individuals under stress and 2) the breakthroughs in senescence/aging "intervention" technology involving the organ prodrug strategy to selectively eliminate senescent cells, and the individual prodrug strategy to eliminate senescent cells with single-cell resolution.

Key words: Aging, Senescence, Molecular Probes, Prodrugs, Identification and Intervention

Short CV

Yuan Guo is a professor at the Northwest University, China. She obtained her BSc in 2001 and PhD in 2006 from Northwest University. She spent two years in France, as a Post-doctoral Research Fellow (2012-2014) at Institut de Chimie Organique et Analytique, University of Orleans, UMR CNRS, and was an invited researcher at University of Orleans (2019), France. Her research interests include: chemical biology; molecular probes in biological systems; tracing and intervention of aging/senescence. Since she started her research work independently, more than 70 research papers have been published in academic journals as a correspondent author, including Nat. Aging, Angew. Chem. Int. Ed., Adv. Sci., Chem. Sci., etc. 10 national invention patents have been authorized and two of them have been transferred to companies. In addition, she serves as a member of the editorial board of several journals such as Chinese Chemical Letters, Acta Materia Medica, and Fine Chemicals.

Simultaneous quantitation of persulfides, biothiols and hydrogen sulfide through efficient sulfur exchange reaction with trityl spin probes

Yangping Liu (刘阳平)

School of Pharmacy, Tianjin Medical University, China

Email: liuyangping@tmu.edu.cn

Abstract

Reactive sulfur species (RSS) including persulfides (RSSHs), biothiols (RSHs) and hydrogen sulfide (H2S) are key regulators in various physiological processes. To better understand the symbiotic relationship and interconversion of these RSS, it is highly desirable but challenging to develop analytical techniques that are capable of detecting and quantifying them. Herein, we report the rational design and synthesis of novel trityl radical-based electron paramagnetic resonance (EPR) probes dubbed as CT02-TNB and OX-TNB for various RSS. CT02-TNB underwent fast sulfur exchange reactions with two reactive RSSHs (PS1 and PS2) which were released from their corresponding donors PSD1 and PSD2 to afford the specific conjugates. The resulting conjugates exhibit characteristic EPR spectra, thus enabling the discriminative detection and quantitation of the two RSSHs. Moreover, CT02-TNB showed good response towards other RSS including glutathione (GSH), cysteine (Cys), H2S and sulfite as well. Importantly, based on the updated EPR spectral simulation program, simultaneous quantitation of multiple RSS (e.g., PS1/GSH/Cys or PS1/GSH/H2S) by CT02-TNB was also achieved. Finally, the levels of the released PS1 from PSD1 and endogenous GSH in isolated mouse livers were measured by the hydrophilic OX-TNB. This work represents the first study achieving discriminative and quantitative detection of different persulfides and other RSS by a spectroscopic method.

Key words: persulfide; reactive sulfur species (RSS); redox; electron paramagnetic resonance (EPR); probe

Short CV

Yangping Liu received the PhD degree in Institute of Chemistry, Chinese Academy of Sciences in 2006 and then moved to The Ohio State University as a post-doc and research scientist from 2006 to 2013. In 2013, he joined Tianjin Medical University as a full professor and then promoted to vice dean in School of Pharmacy. Dr. Liu's research interest is to develop novel EPR probes for precise measurement of redox status in biological systems, stable radicals as magnetic resonance-related agents and gas signaling donors for cardiovascular diseases. Dr. Liu is active in the field of free radicals with more than 70 scientific papers. Dr. Liu is currently an executive member of Chinese Society of Free Radical Biology and Medicine and was awarded as Excellent Young Research Award from Xu Yuanzhi Award Funds of EPR Development in 2020.

Spatial transcriptome profiling of a Huntington's disease mouse brain with BASSFISH

Aihui Tang (唐爱辉)

University of Science and Technology of China, China

Email: tangah@ustc.edu.cn

Abstract

Unraveling spatiotemporal dynamics in cells and molecules during disease progression is pivotal for elucidating disease mechanisms. We present BASSFISH, an innovative imaging-based spatial transcriptomics technique that leverages signal amplification and coded multiplex hybridization for rapid, cost-effective acquisition of high-resolution transcriptomics and multi-protein expression data within tissue samples. Our study employed BASSFISH to analyze over 1200 genes and multiple proteins in 6-month-old CAG-140 mice, a Huntington's disease model, using whole-brain sagittal sections. Integrating these findings with single-cell sequencing, we discovered cell-type and regional transcriptomic alterations during the early stages of HD, thereby generating a comprehensive cellular map of disease progression. BASSFISH stands as a powerful instrument for pinpointing the molecular and cellular underpinnings of disease pathology.

Key words: Spatial Transcriptome, FISH, Hunting's disease, imaging

Short CV

Professor at the School of Life Sciences and Medicine, University of Science and Technology of China, and Hefei National Research Center for Physical Sciences at the Microscale; Invesigator at the Institute of Artificial Intelligence, Hefei Comprehensive National Science Center; Recipient of the National Innovation Talent Youth Project.

He has been primarily engaged in the development of single-molecule imaging technology, including superresolution localization microscopy and imaging-based spatial transcriptomics, and their applications in neuroscience. His research in neuroscience focuses on the structural mechanisms of synaptic transmission and plasticity, and the pathogenesis caused by their abnormalities, including significant discoveries such as synaptic nanocolumns. He has published multiple papers in renowned journals including Nature, Nature Methods, PNAS, and Science Advances as the corresponding author.

Generation of short chain aldehydes and increase of oxidative stress in mice by intake of fructose

Kenji Sato

Kyoto University, Japan

Email: kenjisato6213@gmail.com

Abstract

Aldehyde is reactive to amino, imino, guanidyl, and thiol groups, which deteriorates protein function and induce pathological responses such as inflammation, oxidative stress and consequently negative effects on human health. It is well known that alcohol intake produces acetaldehyde in the liver. In addition to alcohol-induced aldehyde, glucose, one of the carbohydrates that is the main source of energy, also contains an aldehyde group. However, most glucose has hemiacetal structure, and the amount of aldehyde derived from glucose in the body is not so high. Meanwhile, it is known that short-chain aldehydes such as glyceraldehyde and methylglyoxal are produced from the metabolic products of monosaccharides. Furthermore, it is known that malondialdehyde and other compounds are produced by the peroxidation of unsaturated fatty acids. Therefore, oxidative stress produces aldehydes. Conversely, it is possible that the generation of aldehydes may cause oxidative stress *in vivo*. However, the effect of the aldehydes generated in body on oxidative stress is not fully understood, as it has been difficult to quantify aldehydes *in vivo*. Recently, we have established a method for the quantitative determination of glyceraldehyde in body (Martin-Morales et al., J. Agric. Food Chem. doi. org/10.1021/acs.jafc.1c03177). We also developed the quantitative stable determination of methylglyoxal and malondialdehyde. As mentioned above, aldehydes are produced by the metabolism of monosaccharides. It has been reported that high intake of fructose damages the functions of the liver and small intestine. Therefore, in this study, we evaluated the production of aldehydes in the body of mice administered glucose and fructose (2 g/kg body weight).

The increase in blood fructose after administration of fructose was much smaller than that after administration of glucose. Unexpectedly, administration of ^{13}C-labeled fructose increased unlabeled glucose in the blood within a few minutes of administration. These results indicate that administration of fructose causes a rapid activation of the gluconeogenesis system. In the liver and kidney, where gluconeogenesis occurs, administration of ^{13}C-fructose significantly increased the production of ^{12}C-methylglyoxal compared with administration of glucose, indicating that methylglyoxal is produced by gluconeogenesis rather than glycolysis. In the small intestine, fructose administration resulted in significantly higher glyceraldehyde production than glucose administration. Administration of ^{13}C-fructose increased ^{13}C-glyceraldehyde in small intestinal tissue and lumen. These results indicate that fructose is metabolized to glyceraldehyde in the small intestine, and some of it leaks into the lumen. Malondialdehyde, a secondary product of lipid peroxidation, was significantly increased in the blood and kidneys by fructose administration compared to glucose administration. This showed that fructose also increases oxidative stress throughout the body.

Fructose administration has been shown to damage liver function and intestinal barrier function. This study revealed that fructose administration increases glyceraldehyde, a metabolic product of fructose, in the small intestine, and further increases methylglyoxal in the liver and kidneys by activating the gluconeogenesis. This suggests that even in cases other than excessive alcohol intake, fructose intake produces highly reactive short-chain aldehydes, which increases oxidative stress in the body and damages organ functions.

Key words: aldehyde, glyceraldehyde, methylglyoxal, fuructose, malodndialdehyde

GSH-induced in situ peptide self-assembly for precise tumor imaging and ROS-based therapy

Yue Yuan (袁月)

University of Science and Technology of China, China

Email: yueyuan@ustc.edu.cn

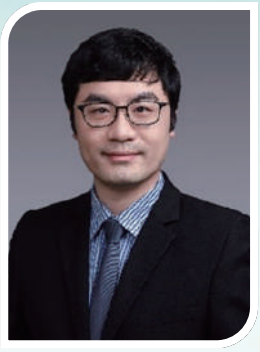
Abstract

Glutathione (GSH) is a key component of the cellular antioxidant system and is the primary nonprotein biothiol found at high concentrations within cells. It plays a crucial role in protecting cellular components from damage caused by reactive oxygen species (ROS) and toxins. In cancer cells, GSH concentrations are approximately 1,000 times higher than in normal cells, making it a significant biomarker for cancer diagnosis. Additionally, combining GSH with other tumor biomarkers, such as proteases and αv integrins, to develop dual-locked responsive probes and drugs can enhance the precision of tumor imaging and treatment. The in situ self-assembly strategy can enable small molecules to specifically accumulate at tumor sites, thereby increasing the local concentration of probes and drugs, improving imaging signals and therapeutic outcomes, and extending treatment duration. In this talk, I will introduce the GSH-responsive in situ peptide self-assembly strategy for enhanced imaging and ROS regulation-based therapy of tumors.

Key words: GSH; peptide self-assembly; tumor imaging; ROS-based therapy

Short CV

Yue Yuan is a Professor in the Department of Chemistry at the University of Science and Technology of China (USTC). She obtained her Ph.D. from the Department of Chemistry at USTC from 2011 to 2015. Following this, she served as a postdoctoral researcher at USTC from 2015 to 2016, and later at the School of Medicine at Johns Hopkins University from 2016 to 2020. She joined USTC in mid-2020. Dr. Yuan′ s current research focuses on redox and protease induced self-assembly for molecular imaging, with particular emphasis on peptide self-assembly for CEST MRI research.



Molecular targeting nano drug candidates

Yang Li (李洋)

Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China

Email: yang.li@siat.ac.cn

Abstract

Currently, the clinical approved nanomedicines are mainly the delivery systems. To develop the nanomedicine that specifically targeting the biomolecules for disease treatment is still a challenging. The study of molecular targeting nanomaterials for drug candidates should be similar to study the small molecule chemical drugs to clearly evaluate and clarify their molecule-targets, revealing the binding sites with a purpose to disclose the potential biological/immunological/pharmacological mechanisms. Therefore, the development of molecular targeting nano drug candidates should be focused on exploring their intrinsic and specific biological properties, which could easily pave the way for future clinical translation. We have discovered several nanomaterials that could specifically/selectively target biomolecules for disease treatments. Black phosphorus (BP) could be used as DNA checkpoint inhibitor to specifically target and inactivate the PLK1 kinase, which consequently causes centrosome dysfunction, mitotic catastrophe, and ultimately leads to cell apoptosis. Thus, BP could be used as a potential anti-tumor drug. CuInP2S6 (CIPS) and cobalt hydroxide nanosheets (CHN) could selectively target the RBD region of SARS-CoV-2 spike protein. Such interaction caused a denaturation of the secondary structure of RBD and occupied the relevant binding sites of RBD-ACE2, thereby inhibiting the infection of SARS-CoV-2 in host cells. Thus, CIPS and CHN could be used as a potential anti-SARS-CoV-2 nano-drug. In addition, based on the three-dimensional structure of the spike protein, the cerium dioxide nanoparticles can selectively target this three-dimensional structure for function inhibition, achieving an effective antiviral effect. These studies revealed that nanomaterials could have specifically/selectively intracellular or extracellular molecular targets, analyzed the nano-bio interfaces and the detailed binding sites, and investigated the valence states of nanomaterials and the spatial effects of proteins for such nano-bio interactions. It clarifies the feasibility of molecular targeting nanomaterials and provides the fundamental strategies for future studies towards this direction.

Key words: Molecular targets, Nano-bio interface analysis, Nanomedicine development

Short CV

His group is now focusing on understanding the basis and mechanism of the nano-bio/immuno interactions and how these interactions modulate the immunological responses. With such basic information, his group is trying to develop efficient nano-formulated medicine to treat infectious/inflammatory diseases and cancer. Prof. Li has published over 50 scientific publications including Nature Nanotechnology (2021, 2022), etc. He awarded the "First Prize of Natural Science in Hebei Province", "Marie Curie Fellowship of European Commission" and "Chinese Government Award for Outstanding Self-financed Students Abroad". Currently, his research team is supported by National Natural Science Foundation of China, National Key R&D Program of China, Natural Science Foundation of Guangdong Province, and funds from Chinese Academy of Sciences, etc.

Nanozybiotics: advancing antimicrobial strategies through biomimetic mechanisms

Lizeng Gao (高利增)

Institute of Biophysics, Chinese Academy of Sciences, China

Email: gaolizeng@ibp.ac.cn

Abstract

Infectious diseases caused by microbes represent a global threat to human health. However, due to the abuse of antibiotics, antimicrobial resistance has evolved rapidly and led to the failure of antibiotics treatment. Thus, alternative antimicrobial strategies different to traditional antibiotics are urgently needed. Lysosomal redox enzymes-based bacteria killing plays a vital role in innate immune defense system, inspiring a novel antimicrobial strategy. However, due to their low stability, potential immunogenicity, and high cost, natural enzymes have limitations in practical antimicrobial therapy. In recent years, many nanomaterials with enzyme-like activities (Nanozymes) have been discovered as a new generation of artificial enzymes which have high activity, high stability, multifunctionality and low cost for large scale. In particular, nanozymes that can mimic the activities of lysosomal enzymes such as oxidase, peroxidase, demonstrated highly antimicrobial effects against pathological bacteria or viruses. To highlight the progress in the field of nanozymes-based antimicrobial strategy (Nanozybiotics), we summarized the antimicrobial mechanisms of action, versatile therapeutics and translational potentials of nanozybiotics in various infectious diseases. We believe that nanozybiotics will provide a new strategy by mimicking immune defense using nanozymes to combat antimicrobial resistance.

Key words: Nanozymes, Lysosome Redox, Biomimetic, Antimicrobial resistance, Nanozybiotics

Short CV

Lizeng Gao is a professor at Institute of Biophysics, Chinese Academy of Sciences (CAS). His research focuses on discovering intrinsic biological activities of nanomaterials (nanozymes) and developing biomimetic strategies against antimicrobial resistance including bacteria, fungi and viruses.

Symposium-YIO-5(Y-5)

"Discovery of new molecules in redox network
Natural products and nutrition in anti-aging and health management"

Chair: Jun Lu (陆军)

Southwest University, China

Email: junlu@swu.edu.cn

Short CV

Prof. Dr. Jun Lu earned, from Sichuan University, his B.Sc. in Chemistry and his M.Sc. in Bioinorganic Chemistry in 1992 and 1995 respectively. He received his Ph.D. in Chemistry from the Changchun Institute of Applied Chemistry, Chinese Academy of Sciences in 1998. He had worked in The Institute of Physical and Chemical Research (RIKEN), Japan from 2000 to 2002, Karolinska Institutet, Sweden from 2003 to 2016. He currently works as the Director of the Teaching and Research in Pharmacology Section, College of Pharmaceutical Sciences, Southwest University, China. Additionally, he is a member of the editorial board of Antioxidants, Frontier in Physiology, and so on. He has published more than 70 scientific papers with a H-index of 40. His current research interests include the study of the mechanism and development of drugs based on targeting the regulation of thiol redox system, and the novel biopharmaceutical technology.

Website:

http://pharmacy.swu.edu.cn/info/1019/2117.htm;

http://pharmacy.swu.edu.cn/info/1124/3249.htm

ORCID number: 0000-0002-1699-8835

Chair: Ock Jin Park

Hanyang University, Korea

Email: ojpark@hnu.kr

Short CV

1966 -1970 Seoul National University College of Pharmacy B.S.

1970 - 1977 University of Minnesota Nutrition M.S. and Ph.D. Candidate

1984 - 1988 Ewha Womans University Nutrition Ph.D.

1980 - 2013 Hannam University College of Bionanoscience: Assistant Professor, Associate Professor, Full Professor

2013 - present Hannam University College of Bionanoscience: Honorary Professor

2021 - present Hanyang University Consulting Researcher

1980 - 2013 Korea Nutrition Society Member, Advisory Board Member and Scientific Committee Member

2001 - 2013 Korean Society of Cancer Prevention Member, Advisory Board Member, Vice President and Scientific Committee Member

2001 - 2013 Members of SFRR of Korea, Korea Toxicology Society, Korea Biomedical and Biochemistry Society, Korea Biochemistry and Molecular Biology

Targeting DNA repair to extend lifespan

Zhiyong Mao (毛志勇)

Clinical and Translational Research Center, Shanghai First Maternity & Infant Hospital, Tongji University, China

Email: zhiyong_mao@tongji.edu.cn

Abstract

Oxidative stress induces various DNA damages, and efficient repair is vital for delaying aging and preventing age-related diseases. While DNA repair deficiencies are known to hasten aging, targeted DNA repair for anti-aging purposes is an underexplored area. Our identification of several potential targetable DNA repair factors that could slow aging provides a theoretical basis for developing strategies to extend healthy lifespan. These factors may include specific repair enzymes or regulatory proteins, offering new avenues for interventions to enhance DNA repair and promote longevity.

Key words: DNA repair and aging

Short CV

• ACADEMIC EDUCATION:

Ph.D. Biology, University of Rochester, USA, 2010

M.S. Biology, Nanjing University, China, 2004

• RESERCH & PROFESSIONAL EXPERIENCE:

2012-present Professor, Tongji University, China

2010-2012 Postdoc, University of Rochester, USA

• MAJOR RESERCH INTERESTS:

DNA repair and aging

Redox-regulated iron metabolism and ferroptosis in ovarian cancer: molecular insights and therapeutic opportunities

Jinzhi Lu (鲁锦志)

Department of Laboratory Medicine, The First Affiliated Hospital of Yangtze University, China

Email: jinzhilu2015@yeah.net

Abstract

Ovarian cancer (OC), known for its lethality and resistance to chemotherapy, is closely associated with iron metabolism and ferroptosis—an iron-dependent cell death process, distinct from both autophagy and apoptosis. Emerging evidence suggests that dysregulation of iron metabolism could play a crucial role in OC by inducing an imbalance in the redox system, which leads to ferroptosis, offering a novel therapeutic approach. This review examines how disruptions in iron metabolism, which affect redox balance, impact OC progression, focusing on its essential cellular functions and potential as a therapeutic target. It highlights the molecular interplay, including the role of non-coding RNAs (ncRNAs), between iron metabolism and ferroptosis, and explores their interactions with key immune cells such as macrophages and T cells, as well as inflammation within the tumor microenvironment. The review also discusses how glycolysis-related iron metabolism influences ferroptosis via reactive oxygen species. Targeting these pathways, especially through agents that modulate iron metabolism and ferroptosis, presents promising therapeutic prospects. The review emphasizes the need for deeper insights into iron metabolism and ferroptosis within the redox-regulated system to enhance OC therapy and advocates for continued research into these mechanisms as potential strategies to combat OC.

Key words: redox, iron metabolism, ferroptosis, ovarian cancer, tumor immune microenvironment, glycolysis

Short CV

Dr. Jinzhi Lu is an active researcher in the field of oncology, with a specific focus on ovarian cancer and the mechanisms of chemotherapy resistance. His academic interests lie in iron metabolism, oxidative stress, and the role of signaling pathways in cancer stem cell formation and drug resistance, particularly in relation to cisplatin. He has led and participated in multiple funded research projects, including studies on the mechanisms of ferroptosis and the regulatory roles of proteins like HIF-1α in ovarian cancer.Dr. Lu has authored numerous impactful publications in high-ranking journals, contributing to the understanding of TRAIL receptors in early pregnancy loss and the identification of critical genes for cisplatin resistance. His work contributes to the advancement of scientific knowledge and may help inform potential therapeutic interventions in cancer treatment.

Restored PGAM5-mediated oxeiptosis eliminates ROS high cardiomyocytes and improves cardiac function during cardiac aging

Moshi Song (宋默识)

Institute of Zoology, Chinese Academy of Sciences, China

Email: songmoshi@ioz.ac.cn

Abstract

Cardiac aging is a major risk factor of CVDs as the incidence of cardiovascular disease as well as the rate of cardiovascular mortality and morbidity increase exponentially in the elderly population. It has been well established that cardiomyocyte death executed by diverse forms of cell death are linked with the adverse outcome of aged heart, it is unclear whether a certain form of cardiomyocyte death may serve a protective role in aged hearts. Here, we explored the role of PGAM5 and its mediated oxeiptosis in cardiac aging. We observed a decrease in PGAM5 levels in aged hearts. Further investigation in a cardiomyocyte-specific Pgam5 knockout (Pgam5 KO) mouse model revealed premature cardiac aging, characterized by increased oxidative stress and an accumulation of ROS high cardiomyocytes. In vitro and *in vivo* analysis revealed that Pgam5 KO led to the inhibition of oxeiptosis in cardiomyocytes. Specifically, we discovered that aged hearts exhibited suppressed PGAM5-mediated oxeiptosis, leading to the accumulation of ROS high cardiomyocytes. Subsequently, we found that restoring PGAM5-mediated oxeiptosis not only eliminated ROS high cardiomyocytes but also significantly improved cardiac function in aging hearts. Collectively, these findings underscore the role of PGAM5-mediated oxeiptosis in maintaining cardiac health and suggest potential therapeutic strategies for combating cardiac aging.

Key words: PGAM5, Cardiac Aging

Short CV

Prof. Moshi Song is a principal investigator in the Institute of Zoology of the Chinese Academy of Sciences. Prof. Song got her master's degree at Karolinska Institute (Sweden) and her Ph.D. at Washington University in St. Louis (USA), received her postdoctoral training at Stanford University (USA), and joined the Institute of Zoology as the leader of the Group of Mitochondrial Disease in 2018. Prof. Song has been focusing on the study of mitochondrial regulation of cardiac aging and related diseases and has published 44 papers in SCI journals including Cell, Cell Research (x2), Advanced Science (x2), Nature Communications (x2), Nature Aging (x2), Nucleic Acids Research (x2) during the last five years. Her major findings are as follows: 1) Elucidation of molecular mechanisms of cardiac aging; 2) Uncover of new biomarkers of cardiac aging; 3) Establishment of interventive strategies for cardiac aging and related diseases.

Exploring the neuroinflammatory pathways of 8-oxoGTP and their effects on cognitive decline

Jin Li (李瑾)

The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital/National Center of Gerontology of National Health Commission, Beijing, China

Email: niyani88@126.com

Abstract

Neuroinflammation mediated by continuously activated glial cells may play a core role in neurodegenerative processes and cognitive deficits. Oxidative stress (OS) is considered to be one of the main underlying mechanisms of neurodegenerative diseases and is closely related to other pathological events. The cytoplasmic 8-oxoGTP generated by GTP oxidation increased during OS. On the one hand, 8-oxoGTP can serve as a substrate for RNA synthesis and cause RNA oxidation, leading to impaired protein synthesis, on the other hand, it can be used as a small molecule to regulate signaling. Given the susceptibility of 8-oxoGTP, free 8-oxoGTP as a signaling modulator requires more in-depth study. In this study, we administered multiple intracerebroventricular injections of 8-oxoGTP to SAMP8 mice and observed a significantly impaired performance in cognitive in behavioral experiments. Immunohistochemical analysis further demonstrated a marked reduction in the number of neurons in the cortical and hippocampal regions, accompanied by a significant increase in the number of activated microglia and elevated secretion of inflammatory cytokines. Cellular experiments indicated that 8-oxoGTP activates microglia by triggering the MAPK, AKT, and NF-κB signaling pathways, promoting an inflammatory phenotype. This mechanism highlights the critical role of microglia in 8-oxoGTP-induced neuroinflammation. Our study reveals the significant impact of 8-oxoGTP on neuroinflammation and cognitive decline, providing a theoretical foundation for exploring related therapeutic strategies.

Key words: Neuroinflammation, Oxidative stress, 8-oxoGTP

Short CV

Dr. Jin Li graduated from Peking University Health Science Center. Since 2018, she has been working in Beijing Hospital. She conducts research on nucleic acid oxidation and aging and aging-related diseases. She is supported by the National Natural Science Foundation and the Fundamental Research Funds for the Central Universities. She is a youth member of the free radical biology and free radical medicine branch.

ATF-4 and hydrogen sulfide signaling mediate longevity in response to inhibition of translation or mTORC1

Jin Meng (孟劲)

Capital Medical University, China

Email: jin.meng2022@outlook.com

Abstract

The serine/threonine protein kinase complex mTORC1 (mechanistic target of rapamycin complex 1) is a master regulator of growth and metabolism. Inhibition of mTORC1 slows ageing across phyla, in part by reducing protein translation. Various stresses, including oxidative stress, nutrient deprivation, and loss of proteostasis, globally suppress protein synthesis through the integrated stress response (ISR), resulting in preferential translation of the transcription factor ATF-4. Here we show in C. elegans that inhibition of translation or mTORC1 increases ATF-4 expression independently of the canonical ISR signaling. Overexpression of ATF-4 is sufficient to extend healthspan and lifespan. ATF-4 not only activates canonical anti-ageing mechanisms, but also elevates expression of the transsulfuration enzyme CTH-2 to increase hydrogen sulfide (H2S) production. The ATF-4/CTH-2/H2S pathway also mediates longevity and increased stress resistance from mTORC1 suppression. Together, our results suggest that increasing H2S levels, or enhancing mechanisms that H2S influences through persulfidation on protein cysteines, may represent promising strategies for mobilising therapeutic benefits of the ISR, translation suppression, or mTORC1 inhibition.

Key words: aging, hydrogen sulfide, ATF-4, mTORC1

Short CV

2022 - Associate Professor, Capital Medical University

2021 - 2022 Senior Mary K. Iacocca Postdoctoral Fellow

2020 - 2021 Junior Mary K. Iacocca Postdoctoral Fellow

2018 - 2020 Research Fellow, Joslin Diabetes Center, Harvard Medical School

2018 PhD in Cell Biology, Yale University

2012 B.S. in Life Sciences, Peking University

Selective Publications:

[1] Meng, J. & Ferguson, S. M. J Cell Biol (2018).

[2] Meng, J., Fu, L. et al. Nat Commun (2021).

[3] Statzer, C., Meng, J. et al. Nat Commun (2022).

Network medicine landscape on the health-enhancing properties of natural antioxidants

Guozhen Cui (崔国祯)

Zhuhai Campus of Zunyi Medical University, China

Email: cgzum@hotmail.com

Abstract

Natural antioxidants have attracted increasing attention for their potential in promoting health and preventing disease, yet the mechanisms underlying their redox activities and their protective effects remain incompletely understood. Network medicine, an emerging field that analyzes complex molecular interactions, offers a promising framework for uncovering how these compounds function at a systems level. However, a gap exists in integrating network medicine with the study of natural antioxidants, particularly in understanding the molecular networks involved. This study addresses this gap by employing a network-based approach to investigate the interactions between natural antioxidant compounds and key regulatory nodes within biological signaling networks. We focus on the role of these interactions in maintaining cellular redox balance and mitigating the progression of chronic diseases associated with oxidative stress. Our analysis identifies specific compounds, including quercetin, palmitic acid, and linoleic acid, present in camellia oil, which modulate critical metabolic pathways related to phospholipids, fatty acids, and bile acids. These findings demonstrate the potential of network medicine to uncover novel antioxidant therapies and elucidate the molecular mechanisms that confer protection against tissue injury caused by oxidative stress. This study highlights the critical role of network medicine in advancing the understanding of natural antioxidants. Furthermore, it advocates for the integration of comprehensive evaluation criteria including chemical composition analysis, bioactivity assays, and animal study to assess the safety and efficacy of these compounds as health supplements. By bridging the gap between molecular insights and therapeutic applications, our study contributes to the development of innovative strategies for health promotion.

Key words: antioxidant, natural product, network medicine, health promotion

Short CV

Guozhen Cui currently serves as a professor and PhD supervisor at Zhuhai Campus of Zunyi Medical University. He received his PhD degree in Biomedical Sciences from University of Macau in 2013. He His research focused on the pharmacological studies of Chinese herbal medicine and functional foods, using integrated approach combining network medicine framework-based prediction with experimental validation. Dr. Cui has published over 60 papers in SCI-indexed journals and has obtained research fundings from various external agencies and industry partners, including 3 NSFC.

Cellular senescence and rejuvenation

Jing Qu (曲静)

Institute of Zoology, Chinese Academy of Sciences, Beijing, China

Email: qujing@ioz.ac.cn

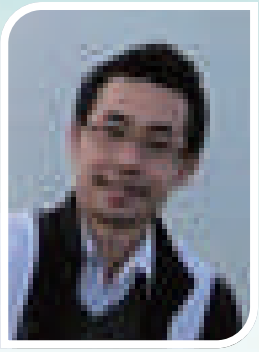
Abstract

In response to a variety of stress factors, certain cells in our organs undergo a transition into a state of senescence, contributing to the accumulation of such cells in different organs as part of the aging process. These senescent cells play a role in the structural and functional decline of organs and are associated with degenerative diseases. Targeting these cells is a critical aspect of the broader strategy to combat aging and help to rejuvenate. However, the heterogeneity of senescent cells and their ambiguous characteristics *in vivo* pose challenges, exacerbated by the lack of efficient methods for their detection and targeted intervention within the body. Dr. Jing Qu is comitted to investigating both the driving causes and *in vivo* impacts of senescent cells. Her research interest is to uncover novel biomarkers and develop intervention strategies to manage cellular senescence and the degeneration in organ structure and functionality.

Short CV

Jing Qu, researcher at the Institute of Zoology, Chinese Academy of Sciences, is mainly engaged in cellular senescence. Cells across different organs undergo a transition into a state of senescence, and the accumulation of such cells in different organs is a part of the aging process. These senescent cells play a role in the structural and functional decline of organs and are associated with degenerative diseases. Jing Qu is committed to investigating the properties of senescent cells, as well as their driving causes. Her research interest is to develop intervention strategies to manage cellular senescence and the degeneration in organ structure and functionality.

Jing Qu received her B.S. from Lanzhou University in 2002, and then the doctor degree from the Institute of Biophysics, CAS in 2007. Following that, she worked as an AFAR Postdoctoral Fellow at the Del E. Web Neuroscience, Aging, and Stem Cell Research Center at the Sanford/Burnham Medical Research Institute, and then as a Research Associate in the Gene Expression Laboratory at the Salk Institute for Biological Studies. In 2014, she initiated her research group focusing on " Stem Cell and Aging"at the Institute of Zoology, CAS. She is now the Chair of the Aging Genetics Elites of the Genetics Society of China, and also a member of Scientific Program Committee of ISSCR. She received the Chinese Young Women in Science Fellowship for her contributions to aging research.



A hybrid sweet potato (Maejo 341) mitigates LPS-induced inflammation and RANKL-induced osteoporosis by regulating ROS-mediated pathways

Chalermpong Saenjum

Faculty of Pharmacy, Chiang Mai University, Chiang Mai 50200, Thailand

Email: chalermpong.saenjum@gmail.com

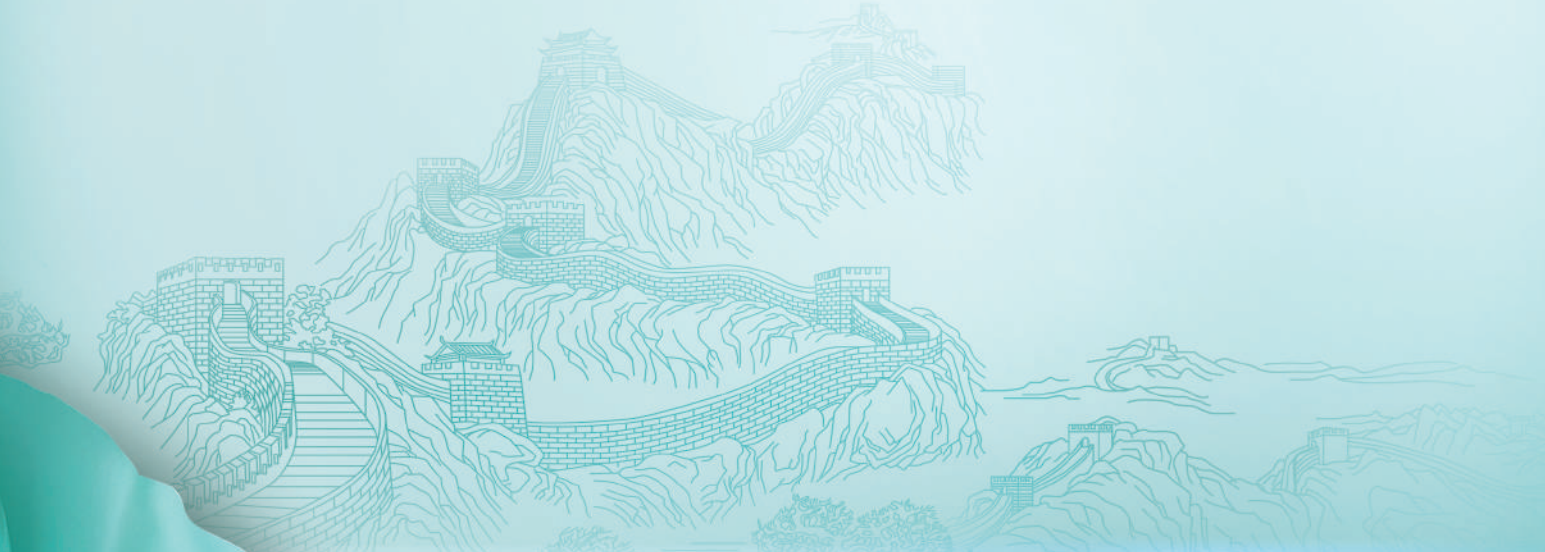
Abstract

"Maejo 341 sweet potato" is one of the new purple sweet potato varieties cultivated in Chiang Mai, Thailand through a crossbreeding of "Phichit 65-3" and "Mun-Khai Sukhothai". However, the health-related impacts of this hybrid crop remain largely unknown. The peel (P) and flesh (F) of Maejo 341 sweet potato were extracted with ethanol (E) and water (W) and denoted as PE, PW, FE, and FW, respectively. The extracts were used to investigate antioxidant, anti-inflammatory, and anti-osteoporotic activities as well as nutritional properties. PE and PW possess a higher phenolic and flavonoid contents, and antioxidant capacity than FE and FW. Therefore, we exclusively chose the peel extracts for further investigations. PE and PW inhibited lipopolysaccharide (LPS)-induced inflammation by suppressing the secretion of nitric oxide and matrix metalloprotein-9 in a dose-dependent manner. PE and PW at 50 mg/mL showed a significant reduction in mRNA levels of representative proinflammatory cytokines, TNF-α, IL-1b, and IL-6, and inhibited expression of two prototypic proinflammatory enzymes, cyclooxygenase-2 and inducible nitric oxide synthase and their mRNA transcripts. PE and PW also induced osteoclast differentiation by suppressing RANKL-stimulated TRAP activity, formation of TRAP-positive multinucleated cells, and expression of TRAP mRNA as well as down-regulation of the osteoclastogenic gene expression. Notably, PE and PW reduced production of reactive oxygen species and enhanced the antioxidant gene expression induced by both LPS and RANKL treatment. Furthermore, PE and PW also stimulated osteogenic activity by inhibiting the TNF-a-mediated decrease in osteoblast viability and alkaline phosphatase activity. The LC-MS and HPLC analyses revealed that the peel extracts contain substantial amounts of anthocyanins, specifically cyanidin-3-O-glucoside, peonidin-3-O-glucoside, and pelargonidin-3-O-glucoside. These compounds are notable for their powerful antioxidant properties, which contribute to anti-inflammatory and anti-osteoporosis effects. All these findings, taken together, suggest the potential use of anthocyanin-enriched Maejo 341 sweet potato peel as an alternative functional food to alleviate oxidative stress- and inflammation-associated osteoporosis, and its ingredients may be developed as the natural pharmaceutical formulations for bone health.

Key words: Maejo 341 sweet potato, Anthocyanins, Osteoporosis, Lipopolysaccharide (LPS), Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL)

Symposium-YIO-6(Y-6)

Redox signaling in organelles/cell fate/development/reproduction



Chair: Zhangjian Huang (黄张建)

China Pharmaceutical University, China

Email: zhangjianhuang@cpu.edu.cn

Short CV

Zhangjian Huang received his B.S. and Ph.D. degrees from China Pharmaceutical University (CPU) in 2004 and 2009, respectively. During 2009 to 2012, he worked as a postdoctoral fellow at University of Alberta in Canada. He joined the Center of Drug Discovery at CPU in 2013. He is now a Professor of Medicinal Chemistry at CPU. His research interests mainly focus on the discovery of novel gaseous signaling molecule nitric oxide (NO)-based agents for the intervention of cardiovascular diseases.

He has published about 80 SCI papers, including 25 in J Med Chem, a top journal in the field of medicinal chemistry. He won Distinguished Professor of the Ministry of Education's "Changjiang Scholars" program in 2024. He has hold 7 funds from National Natural Science Foundation of China including National Natural Science Foundation--Outstanding Youth Foundation (81822041, 2018). In addition, he held Jiangsu Province Funds for Distinguished Young Scientists (BK20160033 in 2016) and Program for New Century Excellent Talents in University (NCET-13-1033, in 2013). He has applied 28 Chinese patents and 10 PCT patent, and obtained 18 authorized patents. He won CPA-Servier Young Investigator Awards in Medicinal Chemistry in 2014.

cxcl18b-defined transitional state-specific nitric oxide signaling drives injury-induced Müller Glia proliferation in the zebrafish retina

Jie He (何杰)

Institute of Neuroscience, Chinese Academy of Sciences

Center for Excellence in Brain Science and Intelligence Technology

Chinese Academy of Science, China

Email: jiehe@ion.ac.cn

Abstract

Zebrafish quiescent Müller glia (MG) can respond to the retina injury by re-entering the cell cycle, a critical step evolutionarily absent from their mammalian counterpart, which is essential for neuron regeneration program. MG could regenerate all retinal fates after the injury in the zebrafish retina by undergoing reprogramming and produced MG derived progenitors. However, the molecular and cellular mechanism driving this species-specific injury-induced MG proliferation may shed the light on new therapeutic strategy to repair human retina diseases but remains largely understood. In our study, single-cell transcriptome analysis reveals the landscape of injury-induced MG state progression from the quiescence to proliferation. We identified the injury-induced MG proliferation via cxcl18b-defined the transitional states. Notably, the cxcl18b-defined MG transitional states recapitulate molecular features of retinal developmental programs. Additionally, we discovered that nos2b is crucial for MG entry into the proliferation via nitric oxides signaling. Cell-specific knockout of nos2b in cxcl18b+ MG significantly reduced the MG proliferation after injury. In conclusion, our findings revealed the novel molecular and cellular mechanisms underlying the transition of MG from quiescence to proliferation after the cone ablation in the zebrafish retina.

Short CV

Dr. He, a researcher at the Center for Brain Intelligence Excellence, Chinese Academy of Sciences. primarily focuses on the generation mechanisms of cell lineage diversity in the central nervous system of vertebrates. Representative achievements include: revealing transcriptional and post-transcriptional regulatory mechanisms governing neuronal type determination across the entire brain; systematically analyzing the lineage structure and developmental program of retinal cell types in neural circuit in zebrafish by combining single-cell multi-omics techniques with *in vivo* cell lineage tracing technology. He has published 16 papers as the first or corresponding author in international academic journals such as Science, Neuron, Journal of Neuroscience, PLOS Biology, Journal of Cell Biology, EMBO Reports, Development, and eLife.

Transforming nutrition into reactive oxygen species for tumor treatment

Peng Huang (黄鹏)

Marshall Laboratory of Biomedical Engineering, International Cancer Center, Laboratory of Evolutionary Theranostics (LET), School of Biomedical Engineering, Shenzhen University Medical School, Shenzhen University, Shenzhen 518055, China

Email: peng.huang@szu.edu.cn

Abstract

Glucose is one of the main energy sources that tumor cells rely on for survival. Glucose oxidase (GOx), an emerging antineoplastic enzyme, has aroused great research interest in metabolism modulation for antitumor therapy due to its inherent biocompatibility and biodegradability, and its unique catalytic properties against β-D-glucose. GOx can effectively catalyze the oxidation of glucose into gluconic acid and hydrogen peroxide. This process depletes oxygen levels, resulting in elevated acidity, hypoxia and oxidative stress in the tumor microenvironment. All of these changes can be readily harnessed to develop a multimodal synergistic cancer therapy by combining GOx with other therapeutic approaches. In this talk, we will highlight our recent efforts on systematic design and construction of functionally specific GOx-based nanomaterials and present representative paradigms for effectively treatment of cancer, through transforming tumor nutrition (Glucose) into reactive oxygen species.

Key words: Reactive oxygen species, glucose oxidase, glucose, antitumor therapy, nanomedicine.

Short CV

Prof. Peng Huang is a Distinguished Professor, Director of Department of Molecular Imaging, Chief of Laboratory of Evolutionary Theranostics, at the School of Biomedical Engineering, Shenzhen University, China. His research interests are including molecular imaging, nanomedicine and theranostics. He has published many papers in this area in top journals such as Nature Biomedical Engineering, Nature Nanotechnology, Nature Communications, Science Advances, Chemical Reviews, Chemical Society Reviews, Accounts of Chemical Research, Advanced Materials, ACS Nano, Angewandte Chemie International Edition, Journal of the American Chemical Society, etc. Starting from 2008, Dr. Huang has authored over 290 peer-reviewed papers, which have received a total citation of > 34,000 times and given him an H-index at 97. He has been selected as a Global Highly Cited Researcher in the field of Cross-Field by Clarivate for four consecutive years (2020-2023).

Mitochondrial dynamics and redox balance control macrophage cell fate

Weihua Yu (于卫华)

Fourth Military Medical University, Xi'an, 710032, P. R. China

Email: yuweihua_fmmu@163.com

Abstract

Macrophages are monocyte-derived innate immune cells that participate in regulating inflammation response and various pathologies. Macrophages are usually divided into two categories, pro-inflammatory (M1) and anti-inflammatory (M2) macrophages. However, the mechanism involved remains obscure. Here, we aim to investigate the role of mitochondrial dynamics and redox balance in regulating macrophage polarization. In LPS-treated macrophages, mitochondria show increased mass, shorten length and looser cristae, which indicated enhanced mitochondrial fission. We prove that mitochondria in M1 macrophages shift their function from ATP synthesis to ROS generation, and ROS modulates NFκB-dependent pro-inflammatory response. Dynamin-related protein 1 (Drp1) is a key GTPase that plays critical role in regulating mitochondrial fission. Our data show that Drp1-dependent mitochondrial fission promotes macrophages pro-inflammatory differentiation. Knockdown or inhibition of Drp1 alleviates LPS-induced macrophages pro-inflammatory differentiation and mice sepsis. As a key member of the STAT family, signal transducers and activators of transcription 2 (Stat2) is indispensable for IFN-mediated anti-viral and anti-tumor. We prove that Stat2 enhances LPS-induced mitochondrial fission through regulating Drp1 S616 phosphorylation. Knockdown of Stat2 blunts the increase of pro-inflammatory cytokines in LPS-stimulated macrophages. Therefore, these results suggested that Stat2-Drp1 mediated mitochondrial fission modulates the initiation of macrophage pro-inflammatory response. Moreover, we observe an obvious increase of mitochondrial fusion and decrease of ROS generation in IL4-activated M2 macrophages. Enhance mitochondrial fusion also promotes the expression of anti-inflammation cytokines, including Arg1, Fizz1 and IL-10. It has been reported that ROS dose influences the inflammatory course, and ROS reduction promotes macrophages anti-inflammatory response. Hence, we prove that mitochondrial fusion boosts anti-inflammatory response through inhibiting mtROS generation. In conclusion, the crosstalk of mitochondrial dynamics and redox signaling may control macrophages polarization. Increased mitochondrial fission and ROS generation facilitates M1 macrophages pro-inflammatory response, while enhanced mitochondrial fusion and decreased ROS promotes M2 macrophages anti-inflammatory response.

Key words: Redox balance, Inflammation, macrophage, mitochondrial dynamics

Short CV

Yu Weihua, born in February 1988, Ph.D., is director and associate professor of the Toxicology Department of the Fourth Military Medical University.

Mitochondrial superoxide stress response: implications for aging and health

Ye Tian (田烨)

Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, China

Email: ytian@genetics.ac.cn

Abstract

Mitochondria play pivotal roles as both energy producers and signaling centers within cells, profoundly impacting metabolism and aging through intricate communication with the nucleus. The maintenance of nuclear envelope (NE) integrity is crucial for cellular function, yet the mechanisms underlying its preservation during aging remain elusive. Here, we demonstrate that inhibiting mitochondrial electron transport chain (ETC) activity preserves NE integrity in aging Caenorhabditis elegans. Reduced ETC activity triggers elevated levels of mitochondrial superoxide, inhibiting polyunsaturated fatty acid (PUFA) biosynthesis through SBP-1-mediated lipid metabolism regulation. The lipidomic analysis uncovers a widespread reduction in PUFA, leading to diminished lipid peroxidation in organisms with elevated mitochondrial superoxide. Dietary supplementation of PUFAs abolished the NE protection. Moreover, interventions targeting lipid peroxidation effectively preserve NE integrity in monkey Hutchinson-Gilford Progeria Syndrome (HGPS) models and human BJ senescent cells. Additionally, we introduce an open platform utilizing image-based artificial intelligence (AI) algorithms for quantitative assessment of NE morphology. Thus, our work unveils unexplored mitochondria-NE crosstalk and underscores lipid peroxidation's pivotal role in NE integrity regulation and cellular aging.

Key words: Mitochondrial Superoxide Stress, Lipid homeostasis, Membrane integrity, Aging

Short CV

Dr. Ye Tian earned her B.S. degree in Biotechnology from Beijing Normal University in 2005, followed by a Ph.D. degree in Biochemistry and Molecular Biology from a joint program of Beijing Normal University and the National Institute of Biological Sciences, Beijing in 2010. Her academic journey continued with postdoctoral training at the Salk Institute and the University of California, Berkeley from 2010 to 2016. In 2016, she assumed the role of Principal Investigator at the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing.

Her research focuses on the regulatory mechanisms of mitochondrial stress and aging, resulting in several achievements. These include the discovery that neuronal mitochondria can transmit "stress memory" across generations by increasing mitochondrial DNA copy numbers in germ cells, enhancing offspring stress resistance and lifespan. Additionally, her work identified various cross-tissue mitochondrial signal exchanges influencing overall metabolism and aging. Furthermore, she uncovered the role of mitochondrial metabolites in regulating aging through epigenetic factors, providing a theoretical foundation for targeting metabolites to mitigate aging.

The ER redoxtasis: from basic research to the intervention of aging and diseases

Lei Wang (王磊)

Institute of Biophysics, Chinese Academy of Sciences, China

Email: wanglei@ibp.ac.cn

Abstract

The unique oxidizing environment of the endoplasmic reticulum (ER) facilitates the oxidative folding of secretory and membrane proteins, which are rich in disulfide bonds. The endoplasmic reticulum (ER) oxidoreductin-1α (Ero1α) and protein disulfide isomerase (PDI) constitute the pivotal oxidative protein folding pathway in the ER. Our previous work has shown that oxidative protein folding fidelity and ER redox homeostasis (redoxtasis) are maintained by both the precise control of Ero1α oxidase activity and the division of labor between PDI family members. Deregulated Ero1α-PDI functions contribute to aging and various diseases including cancers, thrombosis and inflammation. Our recent work identified two small molecule compounds, from an FDA-approved drug library, as highly selective Ero1α-PDI inhibitor, which providing new strategies for combating diseases associated with ER redox dysregulation.

Key words: ER, redox, disulfide bond, aging, disease

Short CV

Prof. Lei Wang is a Principal Investigator at the National Laboratory of Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences. His research focuses on the ER homeostasis and human health, including the mechanism of oxidative protein folding and redoxtasis regulation in the ER, and their roles in aging and related diseases. He has published more than 40 research and review papers in peer-reviewed journals.

Regulation of plant development by peptides–receptor kinases–ROS signaling

Chao Li (李超)

School of life sciences, East China Normal University, Shanghai, China

Email: cli@bio.ecnu.edu.cn

Abstract

In angiosperms, successful sexual reproduction relies on complicated communications between male and female organs. In the study of pollen-stigma interaction, we established a lock-and-key mechanism that before pollination FERONIA receptor kinase and its homolog ANJEA (FER–ANJ) perceives the RAPID ALKALINIZATION FACTOR peptides RALF23/33, inducing the generation of reactive oxygen species (ROS) in stigma papillary cells via a ROP2–RBOHD pathway; during pollination, the POLLEN COAT PROTEIN B-class peptides (PCP-Bs) compete with RALF23/33 for binding to FER–ANJ, leading to a reduction in stigmatic ROS and subsequently facilitating pollen hydration. This study underscores the precise regulation of plant development by receptor kinases that perceive and switch between different types of peptide ligands. In the study of pollen tube growth, we found that GPI-anchored proteins LLG2/3 act as chaperones to facilitate the trafficking of AUX/BUPS receptor kinases from the endoplasmic reticulum to the plasma membrane of the pollen tube tip region; wherein LLG2/3 serve as coreceptors of ANX/BUPS receptor kinases to perceive the RALF4/19 peptides and activate a RAC/ROPs–NADPH oxidases–ROS pathway, which assures the cell wall integrity during the fast growth of pollen tubes. Furthermore, we demonstrate that auxin regulate the production of ROS and nitric oxide (NO) through FER receptor kinase–NADPH oxidase signaling pathway. Interestingly, ROS and NO initiate oxidative modifications in TIR1$^{C140/516}$ and AFB2$^{C135/511}$, facilitating their subsequent nuclear import. The oxidized forms of TIR1$^{C140/516}$ and AFB2$^{C135/511}$ play a crucial role in enhancing the function of TIR1 and AFB2 as auxin receptor in transcriptional auxin responses. These studies shed light on the complex signaling networks and molecular mechanisms that drive plant development, offering fresh insights into how receptor kinases, peptide ligands, and oxidative signaling work together to regulate essential developmental processes in plants. <Liu C, et al. Science. 2021; 372:171; Lu B, et al. Mol Plant. 2024; 17:772; Feng H, et al. Mol Plant. 2019; 12:1612.>

Key words: CrRLK1L receptor kinase, RALF peptides, reactive oxygen species, oxidative modification, plant development

Short CV

Prof. Chao Li, head of the Botany Department at the School of Life Sciences, East China Normal University. She has received several prestigious awards, including the Wei-Zhiming Young Innovation Award (CSPB), the Rising Star Award (SSBMB), and Shanghai Eastern Scholar Elite Program. She earned her Ph.D. from the Institute of Genetics and Developmental Biology, CAS and completed postdoctoral research at the University of Massachusetts. Since 2016, he has led an independent research group focusing on peptides-receptor kinases and plant development, with key findings published in top journals such as Science, Mol Plant, eLife.

Reciprocal role of the Keap1-Nrf2 pathway in the self-renewal and differentiation of airway stem cells and tongue stem cells

Youngtae Jeong

DGIST, Korea

Email: jyt@dgist.ac.kr

Abstract

Mutations in the Keap1-Nrf2 pathway occur in more than 30% and 10% of lung and head and neck squamous cell carcinomas, respectively. However, the role of the Keap1-Nrf2 pathway in the stem cells in the airway and oral cavity, where those cancers are frequently found, has yet to be discovered. Here, we report the reciprocal role of the Keap1-Nrf2 pathway in regulating airway and tongue stem cell self-renewal and differentiation. To facilitate airway stem cell research, we established the tracheal organoid system and developed the airway stem cell-specific lineage tracing system, which revealed that the Keap1-Nrf2 pathway promotes airway stem cell self-renewal. We also established the tongue organoid system and a chemical tongue injury-recovery mouse model. In contrast to the airway stem cells, the Keap1-Nrf2 pathway promotes tongue stem cell differentiation. Further studies to elucidate these tissue-specific differences are currently ongoing. These data indicate that the Keap1-Nrf2 pathway has differential regulatory roles in stem cells in each tissue, which should be considered in developing regenerative medicine by modulating the Keap1-Nrf2 pathway in each tissue.

Key words: Keap1-Nrf2 pathway, airway, tongue, self-renewal, differentiation, stem cells

Involvement of UVB/ROS-mediated signaling pathway in karyoptotic cell death

Yong-Yeon Cho

The Catholic University of Korea, Korea

Email: yongyeon@catholic.ac.kr

Abstract

Intracellular organelles enclosed by membranes play critical roles in maintaining cellular homeostasis. The nucleus, the largest organelle in the cell, is composed of two lipid bilayers and houses genomic DNA, where genetic information is stored. To accommodate the extensive length of genomic DNA within the confined space of the nucleus, it must be tightly packaged and highly organized. However, the nucleus is subjected to expansion pressure due to this tightly packed DNA, and any disruption in the forces counteracting this pressure can lead to a loss of nuclear integrity and ultimately, cell death. While cancer cells often develop resistance to apoptotic cell death, they may remain vulnerable to alternative forms of regulated cell death (RCD). Understanding these additional mechanisms is crucial for developing new therapeutic strategies.

Karyoptosis is a recently proposed form of RCD characterized by nuclear shrinkage, cytoplasmic atrophy, and abnormal nuclear morphologies such as herniations, folds, crevices, fragments, and lobules. This process, distinct from apoptosis and autophagy, involves the excessive excretion of nuclear components and is associated with terminal degradation events in cells. However, the intrinsic factors, extrinsic stimuli, and molecular mechanisms that trigger karyoptosis remain largely unknown.

Our current research has uncovered that cyclic AMP response element-binding protein 3 (CREB3), traditionally recognized as an endoplasmic reticulum (ER)/Golgi-bound transcription factor, plays a pivotal role in this process. We found that CREB3-FL (full-length CREB3) is a type II membrane protein located at the inner nuclear membrane, where it undergoes cleavage by site-1 protease (S1P) and site-2 protease (S2P) to produce CREB3-CF (cleaved form). This cleavage event untethers CREB3-FL from the nuclear membrane, disrupting the balance between the outward expansion force of packed DNA and the inward force exerted by the nuclear membrane. As a result, the nuclear membrane undergoes explosive rupture, abnormal folding, and eventual herniation of nuclear DNA into the cytoplasm, leading to cell death.

Importantly, our findings suggest that karyoptosis can be modulated by external stimuli and by regulating the stability of CREB3. These insights reveal that targeting the regulatory mechanisms governing CREB3-CF accumulation and CREB3-FL cleavage could offer a novel therapeutic strategy to induce karyoptosis in cancer cells, providing a potential new avenue for cancer treatment.

Key words: CREB3, Nuclear membrane rupture, chromatin untethering, karyoptosis, regulated cell death

Symposium-13 (S13)

Redox and neural function & mental health

Chair: Lin Mei (梅林)

Institute of Biomedical Engineering, Peking Union Medical College & Chinese Academy of Medical Sciences, China

Email: meilin@bme.pumc.edu.cn

Short CV

Lin Mei is a professor of Institute of Biomedical Engineering, Peking Union Medical College & Chinese Academy of Medical Sciences. He serves as principal investigator of State Key Laboratory of Advanced Medical Materials and Devices, and director of Tianjin Key Laboratory of Biomedical Materials. His research interests are focused on nanomedicine, molecular pharmaceutics and drug/gene delivery. He has published more than 180 SCI-indexed papers in such top journals as Science Translational Medicine, Nature Communications, and Science Advances, among which there have been 26 ESI-Highly Cited papers. He is also an associate editor of Smart Materials in Medicine and VIEW.

Flavin adenine dinucleotide metabolism and related neuromuscular disorders

Chuanzhu Yan (焉传祝)

Qilu Hospital of Shandong University, China

Email: czyan@sdu.edu.cn

Abstract

FAD and the flavoproteins it supports are involved in a number of catabolic pathways which all converge on the mitochondrion.The re-oxidation of FADH2 from fat oxidation and branched anmino acid catalysis is mediated by the ETF-ETFQO system. Genetic defects in ETFA, ETFB and ETFDH result in multiple acyl-CoA dehydrogenation deficiency (MADD).On the other hand, disturbance of FAD homeostasis caused by genetic defect of riboflavin transporter (RFVT1-3), mitochondrial folate/FAD transporter (MFT) and FAD synthase (FADS) may lead to neuromuscular disorders biochemically mimicking MADD(MADD-like disorders）. Of note, recent reports showed that variant COASY gene codes Coenzyme A synthase and sertroline medication may also cause MADD-like phenotypes. Fortunately most patients with MADD or MADD-like disorders, except for MADD type1 and type2, are responsive to riboflavin. While nearly 200 flavoproteins have hitheto been identified, FAD homeostasis and re-oxidation of FADH2 may play an important role for cell metabolism and energy production. We advocate a collaborative study launched by clinical doctors and scientists in the field of redox biology and discover more potential disorders potentially related to FAD metabolism.

Short CV

- Professor and Chair of Department of Neurology and Neuromuscular Center in Qilu Hospital of Shandong University.
- President of Chinese Society of Neuromuscular Disorders
- President of China Alliance for Rare Diseases of Neurological Rare Diseases
- Vice president of Chinese Society of Neurology
- Broad member of AOMC(Asian and Oceanian Myology Center)

In-situ fluorescence imaging of brain disease-associated bioactive molecules

Ping Li (李平)

Shandong Normal University, China

Email: lip@sdnu.edu.cn

Abstract

Brain diseases such as stroke and depression have a very high incidence and death and disability rates, bringing great mental and economic burdens to families and society. To effectively prevent and treat brain diseases, we must have a thorough understanding of the occurrence and development of brain diseases. However, at present, brain diseases have been a major challenge in the field of neuroscience due to their complex pathogenic factors, unclear etiology, and unknown pathogenesis. Existing findings suggest that bioactive molecules, including neurotransmitters, corresponding synthetic or hydrolytic enzymes, reactive oxygen radicals (ROS), reactive nitrogen radicals (RNS), and metal ions, play a crucial role in developing depression and stroke. To address the current bottleneck in detecting brain disease-related bioactive molecules in neurons in the living brain, we have developed a series of organic small molecule two-photon fluorescent probes that are stable, biocompatible, and fast-responding, and have realized the detection of ROS (hydroxyl radicals, superoxide anion radicals), neurotransmitter hydrolases (acetylcholinesterase), and metal ions (zinc ions), etc., in the cells of neurons in the living brain. Highly sensitive and specific two-photon fluorescence imaging analysis has systematically investigated the changes of disease-related bioactive molecules in mouse brain *in vivo* and preliminarily explored the related signaling pathways involved in the active molecules, which will provide important information and an ideal imaging probe for the study of molecular mechanisms related to the onset and development of depression and stroke.

Key words: Brain diseases, ROS, fluorescence imaging

Short CV

Ping Li obtained her doctorate degree from Shandong Normal University in 2008. Since 1998, she has been working at the College of Chemistry, Chemical Engineering and Materials Science, Shandong Normal University. Currently, she is a second-level professor, doctoral supervisor, and a member of the university's academic committee. She enjoys the special allowance of the State Council, is selected for the National Hundred, Thousand, and Ten Thousand Talent Program, is recognized as a young and middle-aged expert with outstanding contributions at the national level, is a specially appointed professor of Taishan Scholars, and serves as the leader of the innovation team under the "Changjiang Scholars and Innovative Research Teams in Universities" Program of the Ministry of Education. She is also a member of the 7th Committee of Shandong Provincial Committee of the China Zhi Gong Party, the principal of the Shandong Normal University Basic Committee of the China Zhi Gong Party, and a member of the Shandong Provincial Committee of the Chinese People's Political Consultative Conference.

Mechanisms of α7 nicotinic acetylcholine receptor in modulating inflammatory lung injury and infection

Lin L. Mantell

Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, St. John's University, Queens, NY, USA

Email: mantelll@stjohns.edu

Abstract

Supraphysiological concentrations of oxygen (hyperoxia) can compromise host defense, and increase susceptibility to bacterial and viral infections, causing ventilator-associated pneumonia (VAP). Compromised host defense and inflammatory lung injury are mediated, in part, by oxidative stress in the immune cells and high extracellular concentrations of HMGB1. Here, we report that agonists of α7 nicotinic acetylcholine receptor (α7nAChR), can significantly decreased animal mortality and markers of inflammatory injury in mice exposed to hyperoxia and subsequently infected with Pseudomonas aeruginosa. They can significantly decrease hyperoxia-induced extracellular HMGB1 accumulation and HMGB1-induced macrophage phagocytic dysfunction. Hyperoxia-compromised macrophage function was correlated with impaired mitochondrial membrane integrity, increased superoxide levels, and decreased manganese superoxide dismutase (MnSOD) activity. This compromised MnSOD activity is due to a significant increase in its level of glutathionylation. The α7nAChR agonists significantly decreases the levels of glutathionylated MnSOD, and restores MnSOD activity and mitochondrial membrane integrity. Overall, our results suggest that neuromodulation of lung inflammation plays a pivotal role in host defense.

Key words: Oxidative lung injury, pulmonary infection, neuromodulation, inflammatory reflex, nicotinic receptor

Short CV

After graduating from Beijing University School of Medicine, Lin pursued PhD at SUNY Stony Brook and trained as a NIH fellow at the Cold Spring Harbor Laboratory. She is a tenured full Professor at St. John's University College of Pharmacy and Health Sciences/Feinstein Institutes for Medical Research, Northwell Health System. She is the treasurer of the Society for Free Radical Research International and the Vice President for Finance and Advocacy of the Society for Redox Biology and Medicine. Her research focuses on the mechanisms underlying oxidative stress-induced lung diseases including cystic fibrosis, supplemental oxygen-induced acute inflammatory injury and secondary infection-induced pneumonia, and the role of neuromodulation in the pathogenesis of the disease.

Symposium-14 (S14)

Intelligence materials for precision redox intervention

Chair: Fangyuan Li (李方园)

Shanghai Jiao Tong University, China

Email: lfy@shsmu.edu.cn

Short CV

Fangyuan Li is a Professor at the Shanghai Jiao Tong University School of Medicine. She is mainly engaged in research on the field of biomaterials, accumulating expertise in nanobiomaterials, molecular imaging, drug delivery, cancer and neurological disorders. In recent years, she has published numerous papers as corresponding/first author in academic journals such as Nature Nanotechnology、Nature Communications、Advanced Materials、Journal of the American Chemical Society、Angewandte Chemie International Edition、National Science Review、Nano Today. She has led projects funded by the National Science Fund for Excellent Young Scholars, the National Key Research and Development Program of China, and the Natural Science Foundation of Zhejiang Province. Prof. Li has been honored with the Outstanding Achievement Award for Female Scientists at the 2022 Biophysical Society Meeting, and recognition for provincial-level online first-class undergraduate courses. She is a secretary-general of the Materials Biology and Intelligent Diagnosis and Treatment Technology Branch of the Biophysical Society of China.

Selected Publications:

(1) An artificial protein modulator reprogramming neuronal protein functions，Nature Communications，2024, 15, 2039.

(2) Ligand-mediated magnetism-conversion nanoprobes for activatable ultra-high field magnetic resonance imaging, Angewandte Chemie International Edition, 2024, e202318948.

(3) Alpha-Synuclein Oligomers Driven T1-T2 Switchable Nanoprobes for Early and Accurate Diagnosis of Parkinson's Disease, Advanced Materials,2023, e2310404.

(4) Highly sensitive diagnosis of extracellular calcium ions associated brain diseases using Ca^{2+}-dependent T2-T1 switchable magnetic nanosensors, Advanced Functional Materials, 2023, 2313286.

(5) An immunomodulatory zinc-alum/ovalbumin nanovaccine boosts cancer metalloimmunotherapy through erythrocyte-assisted cascade immune activation, Advanced Science, 2023, 2307389.

Regulation and restoration of microenvironment homeostasis of intestinal diseases based on nanotechnology

Guangjun Nie (聂广军)

National Center for Nanoscience and Technology, China

Email: niegj@nanoctr.cn

Abstract

The disorder of the intestinal microenvironment often goes with a series of intestine problems, such as functional diarrhea, inflammatory bowel disease (IBD), colon cancer, etc. A long period of disorder in the microenvironment will precipitate the development of significant chronic diseases, potentially posing a grave threat to life. Nanotechnology emerges as a promising avenue for precisely regulating and restoring homeostasis to the intestinal microenvironment, specifically targeting the remediation of compromised intestinal ecology, thereby ushering in novel treatments on intestinal diseases.

IBD is a chronic, recurrent inflammatory disorder of the digestive system. Traditional clinical medications are often limited to alleviating symptoms, yet they are prone to disease recurrence. Long-term treatment with these drugs can further complicate matters by inducing drug resistance, elevating the risk of infections, and even cancer. Recognizing these limitations, our team has developed a series of bioactive nanomaterials that aimed at transcending the boundaries of conventional drug therapy and promoting IBD treatment. The overabundance of reactive oxygen species (ROS) constitutes a pivotal pathological hallmark of IBD. To address this, we formulated an oral nano-antioxidant, SeNG, which targets the inflammatory cells in IBD. SeNG not only directly clears H_2O_2 but also upregulates the Nrf2/HO-1 signaling pathway, and then mitigates intracellular ROS level. Furthermore, we integrated a probiotic membrane into this antioxidant nanostructure, yielding another bionic-nanosystem, SeM@E.M. This system synergistically promotes cellular REDOX equilibrium, modulates the intestinal microbiota, influences the lamina propria immune response, and restores intestinal homeostasis. Recognizing the profound influence of intestinal symbiotic bacteria in the IBD microenvironment, we extended our strategy by precisely inhibiting the respiratory and energy metabolism of IBD-associated enterobacteriaceae using tungsten trioxide nanoparticles, which enhances the therapeutic efficacy against IBD.

Colorectal cancer (CRC), a highly aggressive intestinal malignancy, stands as the third most prevalent cancer worldwide and the second leading cause of cancer-related mortality. Leveraging the physiological features of intestinal tract, our team has developed an oral tumor vaccine that harnesses biologically modified Escherichia coli (E. coli) as a vector for delivering outer membrane vesicles (OMV) vaccine. These engineered bacteria produce OMVs, which express specific tumor antigens directly within the intestinal tract in response to exogenous signals. Subsequently, the OMVs infiltrate the lamina propria, prompting the maturation of

dendritic cells, which subsequently activate T cells to specifically eliminate tumor cells, thereby reinforcing the host's immune memory. In mouse models of subcutaneous colon tumors and lung metastases, this approach significantly suppressed tumor growth, demonstrating its promising potential.

Key words: intestinal disease, microenvironment, nanotechnology, intestinal microbiota

Short CV

Dr. Nie has a long-standing interest in nanomedicine, biomaterials, cancer biology, blood physiology and the pathophysiology of human disorders involving dysregulation of redox balance and metal metabolism. Currently, his main interests are in nanomedicines, nanovaccines and the design of biology-inspired materials to overcome the current barriers in tumor therapy. His group is working toward controlling the chemical properties of multi-functional nanoparticles to allow specific targeting and regulation of tumor cells and their microenvironment.

Dr. Nie's most recent research activity has generated a collection of interdisciplinary works in the fields of nanobiology, nanomedicine and blood physiology, comprising over 330 papers published in Nature Biotechnology, Nature Nanotechnology (2), Nature Biomedical Engineering (3), Nature Communications (5), Nature Protocols (2), Nature Reviews Cancer, Nature Reviews Materials, Science Translational Medicine (2), Cell Chemical Biology, Nature Materials, Acc Chem Res, Adv Mater, Angew Chem, Blood, Biomaterials, Br J Haematol, Cancer Res, Circulation Res, JACS, JBC, JCI, Mol Cancer Ther, Nano Letters and Trends Biotech. Additionally, he has filed over 50 patents on novel nanomedicines, over 30 of which have been granted. Three patents on antitumor drug development have been transferred to 3 biotechnology firms for further development.

Dr Nie was honored as "Fellow of FRSC" (2023), "AIMBE College of Fellows Class of 2022", "The 1st Class, Science and Technology Award, Beijing Municipal Science and Technology Commission", "Honorary Professor of University of Queensland, Brisbane, Australia", "The 2nd Class, Science and Technology Award, Chinese Pharmaceutical Association, China", "Chief Scientist, National Basic Research Program, Ministry of Science and Technology (MoST), China", "Yiling Pharma. Co. Young Scientist Award, Chinese Pharmaceutical Association, China", "Chief Scientist, National Basic Research Program, Ministry of Science and Technology (MoST), China", "Newton Advanced Scholar, Academy of Medical Sciences, UK", "National Distinguished Young Scholar Award, Natural Science Foundation of China", "Associated Full Member, Methodist Hospital Research Institute, Huston, US", "Hundred Talent Program Scholar, Chinese Academy of Sciences, China". He has been appointed as Associate editors or advisory editor for many prestigious academic journals including Nano Letters, Life Medicine, Nano Today, Exploration, Fundamental Research, Science China Chemistry, Materials Today Chemistry, Advanced Drug Development Reviews.

Molecular mechanisms of selenium intervention in metabolic diseases through regulation of redox homeostasis

Jun Zhou (周军)

Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, China

Email: hustzhj@hust.edu.cn

Abstract

Selenium, an essential trace element, plays an important role in the regulation of redox homeostasis and exerts a variety of important biological functions through selenoproteins. Selenium has both antioxidant and pro-oxidant functions, and is closely related to the onset and progression of a variety of diseases, including cardiovascular disease, diabetes, cataract and cancer. This paper describes relevant advances in our laboratory on selenium redox biology and its relationship with metabolic diseases, mainly including (1) the free radical mechanism of the two sides of selenium nutrient and selenium toxicity; (2) the molecular mechanism underlying selenium intervention in metabolic diseases, such as cardiovascular disease, cataract, diabetes, and cancer; (3) the biological functions and molecular mechanisms of selenoprotein S, selenoprotein F, selenoprotein K, and selenoprotein T.

Key words: selenium, selenoprotein, redox homeostasis, metabolic diseases

Short CV

Position: Professor
Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica
School of Chemistry and Chemical Engineering
Huazhong University of Science and Technology
Address: Room A815, Chemistry Building
Huazhong University of Science and Technology
1037 Luoyu Road, Wuhan, 430074, P.R. China
Email: hustzhj@hust.edu.cn

Education:

2010-2011 Postdoc, Oklahoma of University Health Sciences Center, USA
2005-2009 Ph.D., biochemistry and molecular biology, Huazhong University of Science and Technology, China
2000-2003 M.S., inorganic chemistry, Huazhong University of Science and Technology, China
1996-2000 B.S., applied chemistry, Huazhong University of Science and Technology, China

Professional Experience:

2016- Professor, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, China
2010-2016 Associate Professor, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, China
2010-2011 Research Scholar, Department of Medicine, University of Oklahoma Health Sciences Center, USA
2005-2010 Instructor, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, China
2003-2005 Teaching assistant, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, China

Research Areas:

1. The biological functions of selenium/selenoproteins and their roles in health and disease.
2. Molecular pathological mechanisms and therapeutics in dysregulation of glucose and lipid metabolism.

Professional Activities:

Memberships to professional organizations

2018- Member of the Standing Committee of the Biological Trace Elements Branch of the Chinese Biophysical Society
2024- Member of Specialized Committee on Biological Effects of Reactive Oxygen Species, Chinese Society of Environmental Mutagens
2022- Secretary General, Wuhan Academy of Trace Elements and Health
2022- Premium Member of Chinese Chemical Society

Next-generation RNA sequencing-based deep-learning model to predict chemoresistance in high-grade serous ovarian carcinoma

Yong Sang Song

Gynecologic Cancer Center, Myungji Medical Foundation Myungji Hospital, Goyangsi, Gyeonggi-do, 10475, Korea

Email: yssong@snu.ac.kr

Abstract

To fulfill precision cancer medicine in ovarian cancer, precise prediction of chemoresistance and subsequent recurrence is the first step. So we aimed to develop the next-generation RNA sequencing-based deep-learning model predicting chemoresistance risk in high- grade serous ovarian carcinoma (HGSOC).

We perfomed the next-generation RNA sequencing using fresh-frozen chemotherapy-naïve primary ovarian cancer tissues from HGSOC patients (n=86). Patients were randomly divided into training and test sets with a 2:1 ratio. In model development phase, transcriptomic data of both training set and HGSOC patients (n=208) from The Cancer Genome Atlas database were used. Using genes selected by differential gene expression analysis, we constructed and trained a deep neural network (DNN). Multiple DNN models were combined to build average ensemble models, which were further validated using the test set (validation phase). We assessed the predictive performance of the developed models based on the area under the receiver operating characteristic curve (AUC).

All patients in the study population received platinum-based combination chemotherapy: 14 and 72 were identified as chemoresistant and chemosensitive, respectively. Based on the differential gene expression between these two groups, we have identified 31 genes using two distinct methods. Machine learning algorithms were applied to develop and train DNNs of the 31 genes. Then, the five-fold average ensemble models were developed. Among different ensemble models, the chosen model demonstrated high accuracy in predicting chemoresistant cases (AUC, 0.85).

We successfully developed an RNA sequencing-based, deep-learning model to predict chemoresistance risk after first-line platinum-based chemotherapy in HGSOC. These newly developed models would help the individualized management of HGSOC patients. Incorporating targeted agents into the primary treatment and more intensive surveillance might be considered for patients at high-risk of developing chemoresistance.

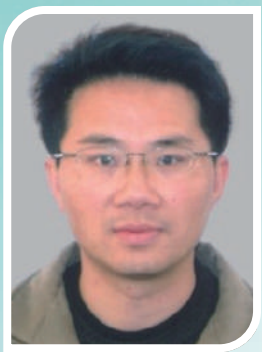
Key words: ovarian cancer; high-grade serous carcinoma; prognosis; chemoresistance; deep learning; model.

Short CV

Prof. Yong Sang Song is Professor Emeritus at Seoul National University, College of Medicine, and currently the Director of the Gynecologic Cancer Center at Myungji Hospital in Republic of Korea. He earned his MD and PhD from Seoul National University in 1983 and 1994, respectively, and served as a professor there from 1994 to 2023. His research focuses on the molecular mechanisms of chemoresistance in gynecologic cancers, particularly ovarian cancer. He has published over 400 papers in SCI journals and serves on the editorial boards of several scientific journals. Prof. Song has received numerous awards for his contributions to cancer research and prevention.

Symposium-15 (S15)

Lifestyle and redox regulation



Chair: Cheng-Gang Zou (邹成钢)

Yunnan University, China

Email: chgzou@ynu.edu.cn

Short CV

Professor Cheng-Gang Zou graduated from Sichuan University with a bachelor's degree, Kunming Medical College with a master's degree, and the University of New England (UNE) with a doctor's degree. After completing postdoctoral training at the University of Nebraska-Lincoln (UNL), he moved to Yunnan University as a Professor in 2004 and now is Donglu Distinguished Professor of Yunnan University. He is currently the deputy director of State Key Laboratory for Conservation and Utilization of Biological Resources, Yunnan University.

Dr. Zou' research interests focus around the mechanism of microbe-host interaction and the role of metabolic pathways in aging. He published more than 50 scientific papers in peer-reviewed journals.

Surplus fatty acid synthesis increases oxidative stress in adipocytes and lnduces lipodystrophy

Tong-Jin Zhao (赵同金)

Fudan University, Shanghai, China

Email: zhaotj@fudan.edu.cn

Abstract

Adipocytes are the primary sites for fatty acid storage, but the synthesis rate of fatty acids is very low. The physiological significance of this phenomenon remains unclear. Here, we show that surplus fatty acid synthesis in adipocytes induces necroptosis and lipodystrophy. Transcriptional activation of FASN elevates fatty acid synthesis, but decreases NADPH level and increases ROS production, which ultimately leads to adipocyte necroptosis. We identify MED20, a subunit of the Mediator complex, as a negative regulator of FASN transcription. Adipocyte-specific male Med20 knockout mice progressively develop lipodystrophy, which is reversed by scavenging ROS. Further, in a murine model of HIV-associated lipodystrophy and a human patient with acquired lipodystrophy, ROS neutralization significantly improves metabolic disorders, indicating a causal role of ROS in disease onset. Our study well explains the low fatty acid synthesis rate in adipocytes, and sheds light on the management of acquired lipodystrophy.

Key words: fatty acid, oxidative stress, adipocytes, lipodystrophy, necroptosis, MED20

Short CV

Professor, Institute of Metabolism and Integrative Biology, Fudan University.

Research Interests

The focus of Zhao laboratory is to understand the underlying mechanism of these metabolic disorders including obesity, diabetes and fatty liver. They focus on: the physiological function of palmitoyl acyltransferases in regulating metabolism; identification of the key factors in adipogenesis and onset of obesity.

Effects of Hyperbaric Oxygen Intervention on Oxidative Stress in the Body after High-Intensity Interval Training

Hao Wu (吴昊)

Capital University of Physical Education and Sports, Beijing, China

Email: wuhao@cupes.edu.cn

Abstract

Purpose: This study aims to explore the impact of HBO intervention on oxidative stress levels following HIIT. Additionally, it seeks to investigate the corresponding mechanisms through the analysis of blood biochemical markers and metabolomics.

Methods: This study recruited 20 healthy male university students who are sports enthusiasts and employed a randomized controlled trial design. The participants were randomly divided into a control group (CON, n=10) and a hyperbaric oxygen group (HBO, n=10). Both groups followed the same exercise training program, with the CON group undergoing natural recovery after training and the HBO group undergoing hyperbaric oxygen recovery post-training. Blood biochemical markers and metabolomics data were collected at different time points before and after the experiment. Results: After the experiment, the SOD levels decreased and MDA levels increased in the CON group, while in the HBO group, SOD levels increased and MDA levels decreased. In terms of metabolomics, significant changes were observed in the metabolic pathways of arachidonic acid metabolism and oxidative phosphorylation. Enriched metabolites in these pathways included arachidonic acid, prostaglandin D2, and leukotriene D4.Conclusions:The HIIT training can induce a certain level of oxidative stress in the body, and HBO may improve oxidative stress levels to some extent, affecting arachidonic acid metabolism and oxidative phosphorylation, thereby reducing oxidative damage and promoting tissue repair.

Key words: hyperbaric oxygen; high-intensity interval training; oxidative stress; metabolomics

Short CV

Professor Wu Hao, Ph.D. in Exercise Physiology, doctoral supervisor. At present, Professor Wu Hao holds the following positions:Director of a key laboratory under the General Administration of Sport of China; Olympic technology expert at the General Administration of Sport of China; Distinguished researcher at the National Institute of Sport Science; Vice President and Secretary-General of the Hypoxia and Health Branch of the Chinese Biophysical Society; Executive Committee Member of the Exercise Physiology and Biochemistry

Branch of the Chinese Society of Sports Science; Vice Chairman of the Beijing Society of Sports Science; Expert Committee Member of the Beijing Health Security Association; Registered health manager; Director of a key laboratory in Beijing; Leader of the academic innovation team for "Strong Teaching of Talents" in Beijing; Deputy Director of the National Sports Industry Research Base; Founder and Curator of the Xuan Culture Museum; Expert Consultant Committee Member of the Beijing Community Sports Association; Co-founder of the Xi'an Rural Development Foundation; Secretary-General of the Collaborative Innovation Center for Sports, Fitness, and Leisure Development in the Beijing-Tianjin-Hebei region; Executive Vice Chairman of the Preservation Association of the Eight Temples outside the Summer Resort in China; National Level I Coach and Referee in Kabaddi.

Research focus on monitoring athletic performance, nutrition, and recovery. Engaged in Olympic research endeavors multiple times, such as serving as the head of the national team's research team during the preparation for the 2008 Beijing Olympics and the 2022 Beijing Winter Olympics, leading to Olympic gold medals and historic breakthroughs. Recognized with accolades including the "Outstanding Individual Contribution to the Beijing Olympics" from the General Administration of Sport of China, the Chinese Olympic Committee, the "Beijing Olympic Merit Award," the "Beijing May 1st Labor Medal," and titles like "Advanced Worker of Beijing."

Experience in teaching undergraduate, master's, and doctoral courses at the university level, covering subjects like "Sports Nutrition," "Specialized Courses in Exercise Physiology," "Youth Physical Fitness Training and Nutritional Recovery," and bilingual courses like "Health Promotion and Weight Control." Supervised and trained over 60 master's and doctoral students. Undertaken and completed various projects including key research and development projects from the Ministry of Science and Technology. Published 25 international SCI papers, authored or co-authored nine books on topics like "Sports Nutrition," "Health Promotion and Weight Control," "Cryotherapy and Exploration of Exercise Capacity," "Kayaking Sports," "Exploration of High-altitude Training in Chinese Rowing Projects," "Vegetarian Sports Nutrition," and "Safe and Effective Exercise for Overweight Adolescents." Holds 1 international invention patent in sports nutrition, 3 national invention patents, 1 utility model patent, and has published 189 papers domestically and internationally.

The role of ileal mucosa -associated microbiota in the patients with Crohn's disease

Osamu Handa

Department of Gastroenterology and Hepatology, Kawasaki Medical School, Kurashiki-city, Okayama, Japan

Email: handao@med.kawasaki-m.ac.jp

Abstract

The intestinal mucus has multiple function of which it protects intestinal epithelial cells from various stimuli in intestinal lumen. Previously we found that aspirin induces small intestinal mucosal injury via superoxide production in mitochondria of small intestinal epithelial cells in vitro <Fukui A. et al. Am J Physiol Gastrointest Liver Physiol 2012. 303: G927-936>. We also found in an *in vivo* mice model that the presence of intestinal mucus significantly reduces the aspirin -induced small intestinal mucosal injury < Suyama Y. et al. Biochem Biophys Res Commun 2018. 498: 228-233>. Although the intestinal mucus itself plays protective role in healthy individuals, however, the microbiota in the intestinal mucus (mucosa -associated microbiota: MAM) plays important role in the pathogenesis of Crohn's disease (CD). In this study, we retrospectively examined the differences in the ileal MAM between CD patients and healthy controls and investigated the factors affecting MAM in CD patients to clarify potential therapeutic targets. As a result, CD patients had significantly reduced α-diversity in the ileum and a difference in β-diversity. The abundance of butyate-producing bacteria in the ileal MAM was significantly lower in CD patients with a history of abdominal surgery than in those without <Handa O. et al. Redox Rep 2023. 28: 2241615>, suggesting the important role of MAM in CD pathophysiology. Because butyric acid is a major energy source in the intestinal epithelium, its metabolism via β-oxidation increases oxygen consumption in epithelial cells, reducing oxygen concentration in the intestinal lumen and increasing the abundance of obligate anaerobic bacteria. The suppression of obligate anaerobes in CD patients caused an overgrowth of facultative anaerobes.

Key words: Crohn's disease, Mucosa -associated microbiota, butyrate, oxygen

Short CV

Osamu Handa is Associate Professor of Department of Gastroenterology and Hepatology, Kawasaki Medical School. He received his MD in 1994, and obtained his PhD in gastroenterology in 2003. He moved to Department of Gastroenterology and Hepatology, Kawasaki Medical School in 2019.

His clinical /basic research field is the oxidative stress in pathophysiology of gastrointestinal diseases. His current interests are (1) inflammatory bowel disease, (2) intestinal mucus, and (3) Helicobacter pylori and gastric carcinogenesis.

Flash Talk-1 (FT-1)

Chair: Suhua Wang (王素华)

Guangdong University of Petrochemical Technology, China

Email: wangsh@gdupt.edu.cn

Ph.D. from the Hong Kong University of Science and Technology and JSPS postdoc fellow. Research interests include basic theories and methods of analytical and bioanalytical chemistry, analysis of environmental pollutants and and detection of free radicals/reactive oxygen/nitrogen species related to life processes and environmental toxicology induction, such as hyroxyl radicals, nitric oxide, and NO_2. He has published over 140 relevant papers in journals including J. Am. Chem. Soc., Anal. Chem. , and Sensors Actuat. B. Chem., and etc.

From target identification to early-stage therapeutic discovery: leveraging in vivo preclinical models

Chair: Ju Cui (崔菊)

Beijing Institute of Geriatrics, National Health Commission, China

Email: cuiju4366@bjhmoh.cn

Short CV

Academic Qualifications

Ph.D. Department of Biochemistry, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, China. Feb. 2011

M.Phil. in Biotechnology, Department of Biology, The Chinese University of Hong Kong, Hong Kong, China. Dec. 2007

B.Sc. in Biotechnology, National Teaching Bases for Life Science and Biotechnology, Department of Biotechnology, Zhejiang University, Hangzhou, China. Jun. 2005

Academic Positions

Professor, The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Beijing Hospital/National Center of Gerontology of National Health Commission, Beijing, China (Jun. 2022-present)

Research Interests

1. Molecular mechanisms and interventions of aging and aging related disease;

2. Cohort study of factors influencing health

Flash Talk-2 (FT-2)

Chair: Yan An (安艳)

Department of Toxicology, School of Public Health

Suzhou Medical College of Soochow University, China

Email: dranyan@126.com

Education

2005	PhD	Environmental Toxicology	Nihon University College of Pharmacy With Prof. Kenzo Yamanaka
2001	PhD	Radiomedicine	Jilin University Norman Bethune Medical College with Prof. Zenglin Gao
1996	MS	Industrial Hygiene and Occupational Diseases	China Institute for Radiation Protection With Prof. Rusong Chen
1993	B.S.Med	Preventive Medicine	Shanxi Medical University

Research statement

I am a toxicologist with a focus on Mechanism and Prevention of Xenobiotics Poisoning, Biochemical and Molecular Toxicology, and The Mechanism of Chemical Carcinogenesis on Redox Stress. I have been conducting the molecular mechanisms of the toxicities of environmental chemicals. Using cell lines and zebrafish embryos as model systems, and dissect the functions of signal pathways. I have raised the hypothesis that the metabolic process associated with the methylation of inorganic arsenicals, the subsequent metabolic sulfurization, and the chemical properties of their intermediate active metabolites play an important role in arsenic-induced Redox-stress Response Capacity in arsenic-induced cell transformation.

Major focuses of my current work are: (1) Regulative role of Redox-stress Response Capacity in arsenic-induced human cell transformation. (2) Environmentally relevant concentrations of chemicals induced developmental toxicity and Redox responses.

Representative Works

1. 'Environmental standard limit concentration' arsenic exposure is associated with anxiety, depression and autism-like changes in early-life stage zebrafish. Journal of Hazardous Material. 2024,469:133953.

2. A Bayesian Benchmark Concentration Analysis for Urinary Fluoride and Intelligence in Adults in Guizhou, China. Science of The Total Environment. 2024: 925: 171326.

3. Reductive Stress Induced by NRF2/G6PD through Glucose Metabolic Reprogramming Promotes to Malignant Transformation in Arsenite-Exposed Human Keratinocytes. Science of The Total Environment. 2023: 896: 165207.

4. Sustained expression of NRF2 and its target genes induces dysregulation of cellular proliferation and apoptosis is associated with arsenite-induced malignant transformation of human bronchial epithelial cells. Science of The Total Environment. 2021, 756: 143840.

Chair: Jinchuan Hu (胡晋川)

Fudan University, China

Email: hujinchuan@fudan.edu.cn

Short CV

Education

2004, Peking University, B.S.

2012, Institute of Microbiology, Chinese Academy of Science, Ph.D.

Work experience

2012-2017, University of North Carolina at Chapel Hill, Postdoc Associate,

2018- , Fudan University, Principal Investigator

Research Interests

1. The roles of DNA oxidative damage in cellular response to oxidative stress, especially how transcription is regulated by DNA oxidative damage during inflammation and other processes.

2. Molecular mechanisms of transcription-coupled nucleotide excision repair which can remove transcription-blocking lesions including oxidative damage.

Representative works

1. Jiao An#, Mengdie Yin#, Jiayong Yin#, ..., Maoxiang Qian*, Jinchuan Hu*. Genome-wide analysis of 8-oxo-7,8-dihydro-2'-deoxyguanosine at single-nucleotide resolution unveils reduced occurrence of oxidative damage at G-quadruplex sites. Nucleic Acids Research, 2021, 49(21): 12252-12267.

2. Jiao An#, Mengdie Yin#, Jinchuan Hu*. G-quadruplex and 8-oxo-7,8-dihydroguanine across the genome: methodologies and crosstalk. Genome Instability & Disease, 2022, 3: 241–254.

3. Liudan Jiang#, Jiayong Yin#, Maoxiang Qian#, ..., Jinchuan Hu*, Honghui Ma*, Yi-Han Chen*. UdgX-Mediated Uracil Sequencing at Single-Nucleotide Resolution. Journal of the American Chemical Society, 2022, 144(3): 1323–1331.

4. Yongchang Zhu#, Xiping Zhang#, Meng Gao#, ..., Jinchuan Hu*. Coordination of transcription-coupled repair and repair-independent release of lesion-stalled RNA polymerase II. Nature Communications, 2024, 15(1): 7089.

5. Yongchang Zhu#, Yuanqing Tan#, Lin Li#, ..., Maoxiang Qian*, Jinchuan Hu*. Genome-wide mapping of protein–DNA damage interaction by PADD-seq. Nucleic Acids Research, 2023, 51(6): e32.

Home page:

https://ibs.fudan.edu.cn/ibsen/05/a5/c39095a460197/page.htm

Chair: Yan Zhao (赵燕)

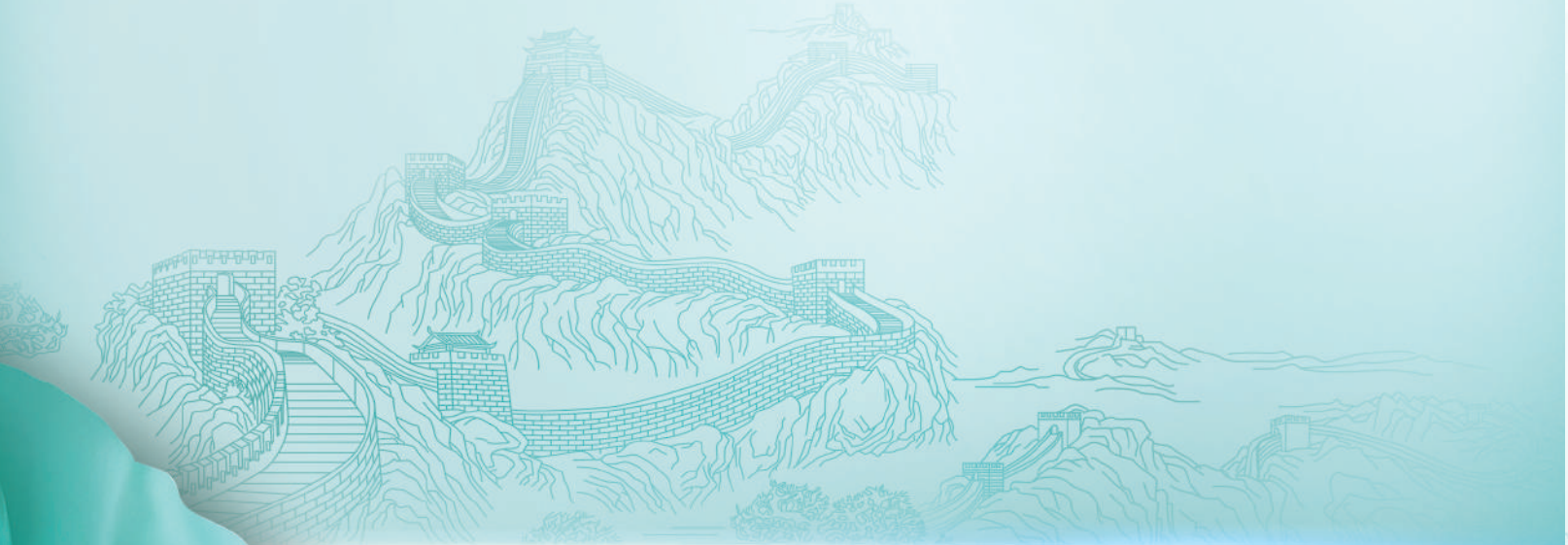
Harbin Institute of Technology (Weihai), China

Email: zhaoyan@hitwh.edu.cn

Short CV

Dr. Yan Zhao is a professor at the Department of Bioengineering, College of Marine Science and Technology, Harbin Institute of Technology (Weihai). She received B.S degree from University of Science and Technology of China, and Ph.D. degree from University of Kentucky. Her current research interest includes nutrition and gene interaction, bioactive compounds in intervention of aging and aging-related diseases.

Flash Talk-3 (FT-3)



Chair: Julia Li Zhong (钟莉)

Chongqing University, China

Email: jlzhonge@cqu.edu.cn

Short CV

Julia Li Zhong (Professor, PhD & MD)

Head of Experimental Dermatology of Chongqing, Chinese Society of Free Radical Biology and Medicine; Chinese Society of Photobiology;

E-mail: jlzhong@cqu.edu.cn; Website: Bioengineering.cqu.edu.cn.

Dr. Julia Li Zhong graduated from Clinical medicine (West China University of Medicine, Sichuan University; Ph.D. in the University of Bath, Photobiology-Pharmacology. Postdoctoral research at Kings College of London & University of London. University of Bath as RA2, 2008; then Chongqing University (Sept. 2009) to carry out teaching & research work. She has presided 4 NSFC(82373501, 2024.1-2027.12), related to UVA effects. & 2023YFC2508200: the National Key Research and Development Program of China.

She has published more than 60 papers in journals such as《Free Radical Biology &Medicine》; 《Oxid Med Cell Longev.》, etc. Moreover, she has joint applied and obtained UVA-LED patents of inventions. She also joint C Pourzand host SKIN@Bath Symposium, 2019, 2023 (China joint) &2024 Bath, UK;

【Research Interesting】

Photobiology. To study UVA radiation human skin cells and mouse model; Skin care (beauty products) & SPA medicine; UVA therapy and drug release: Iron chelation therapy. Skin diseases such as psoriasis and cancer related research etc.

【Publications】

1. Wang M, et al. Zhong JL. Bach2 regulates autophagy to modulate UVA-induced photoaging in skin fibroblasts. Free Radical Biology and Medicine, April, 2021. JCR/Zone2

2. Karisma VW, Wu W, et al Pourzand C, Zhong JL. UVA-Triggered Drug Release and Photo-Protection of Skin. Front Cell Dev Biol. 2021 Feb 11;9:598717.

3. Huang X, Nisar MF, et al, Zhong JL. UV-responsive AKBA@ZnO nanoparticles potential for polymorphous light eruption protection and therapy. Mater Sci Eng C Mater Biol Appl. 2020 Feb;107:110254.

Chair: Junmin Zhang (张军民)

School of Pharmacy & State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China

Email: zhangjunmin@lzu.edu.cn

Short CV

Dr. Junmin Zhang is a Professor in the School of Pharmacy at Lanzhou University. He completed his Ph.D. in Medicinal Chemistry and Biology in 2017 from Lanzhou University, following which he pursued postdoctoral research at the State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Macau (S.A.R.), China. Dr. Zhang is a member of the Chinese Pharmacological Society and Chinese Chemical Society. His research interests lie in the discovery of small molecules that can target cellular redox systems or protein kinases, and their potential therapeutic applications, along with elucidation of their pharmacodynamics and pharmacokinetic mechanisms. Over the past 5 years, he has authored more than 30 papers in reputable Journals such as Trends Pharmacol Sci, Pharmacol Ther, Pharmacol Res, Med Res Rev, J Med Chem, Free Radical Biol Med, and others, either as the first author or corresponding author. His scholarly work has garnered over 1000 citations and includes 2 highly cited papers in the Essential Science Indicators (ESI). Additionally, Dr. Zhang has secured 2 authorized patents, successfully commercialized one, and obtained a registered software copyright. He has led and contributed to several national and provincial scientific research projects. Dr. Zhang's contributions have been recognized with accolades including a first prize for Military Scientific and Technological Progress and two second prizes for Scientific and Technological Progress in Gansu Province. Notably, he was selected for the 2019 International (Overseas) Exchange Program of the National Postdoctoral Management Committee of the Ministry of Human Resources and Social Security, as part of the "Macao Young Scholars Program."

Chair: Kuei-Hung Lai

Graduate Institute of Pharmacognosy, Taipei Medical University, Taiwan, China

Email: kueihunglai@tmu.edu.tw

Short CV

Kuei-Hung Lai is an Associate Professor in the Graduate Institute of Pharmacognosy, Taipei Medical University. After earning a B.S. in Life Science from National Chung Cheng University in 2010, he pursued Ph.D. degree in Pharmacognosy at Uppsala University, Sweden, completing in 2017. Following this, he gained experience in natural products chemistry and analytical chemistry at the National Museum of Marine Biology and Aquarium and the Chang Gung University of Science and Technology. Since 2020, he has been teaching at Taipei Medical University.

With a diverse research training and teaching background in pharmacognosy, he embraces different cultural perspectives to convey scientific knowledge and develop valuable scientific and technological research. Over four years at Taipei Medical University, he and the research team have focused on exploring lead compounds from marine and terrestrial natural products, primarily identifying and evaluating active ingredients with potential therapeutic effects against inflammatory diseases. The team has published 61 SCI papers since 2016, with 832 citations in Scopus and an h-index of 16.

The team also specializes in coral aquaculture, attempting to combine the drug development supply chain by utilizing characteristics of biological competition and defense to stabilize the growth conditions for mass-producing active components from corals sustainably. In recent years, the team has incorporated big data and databases to establish a mass spectrometry analysis application platform, building information on the active metabolic components of traditional Chinese medicine (TCM) and dedicating efforts to evidence-based research in TCM. The team is committed to the value of translational research, having developed a "TCM bioactive metabolite molecular network platform" to identify the active metabolite characteristics of TCM, influencing the selection of key components in Taiwan's TCM guidelines.

In recent years, his academic awards and scholarships include the Ta-You Wu Memorial Award from the National Science and Technology Council in 2024, the Young Scholar Award from the Society of Chinese Natural Medicine in 2023, and the 20th National Innovation Award from the Research Center for Biotechnology and Medicine Policy in 2023.

Poster Location

Venue: The ballroom A	
FT-01	A Chelator-linked Trityl Probe Enabling Highly Specific, Sensitive and Quantitative Detection of Cu(I) by EPR Spectroscopy Yan Wang 王炎 (Tianjin Medical University, China)
FT-02	Deciphering the RSS code in cellular senescence Wong Nai-Kei (Shantou University Medical College, China)
FT-03	Detection and evaluation of novel oxidizing substances in sodium hypochlorite using Trolox Kishimoto Ayuta (Shibaura Institute Of Technology, Japan)
FT-04	High sensitive LC-MS/MS method for determining malondialdehyde in biological sample using thiobarbituric derivatization Ujihara Miyu (Kyoto University, Japan)
FT-05	A novel protein CYTB-187AA encoded by the mitochondrial gene CYTB modulates mammalian early development Zhijuan Hu 胡志娟 (Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, China)
FT-06	A novel redox gene atad-3 identified by whole genome RNAi screening in Caenorhabditis elegans Jiao Meng 孟姣 (Institute of Biophysics, Chinese Academy of Sciences, China)
FT-07	Elucidating the reducibility of sulfur dioxide on cysteine proteomes Zongmin Li 李宗敏 (Peking University First Hospital, China)
FT-08	Exploring the collaboration of redox and autophagy systems based on a genome-wide new redox genes screening Xinhua Qiao 乔新华 (Institute of Biophysics, Chinese Academy of Sciences, China)
FT-09	TRPC6-mediated Zn^{2+} influx improves heart failure through supersulfide formation Xinya Mi (Graduate School of Pharmaceutical Sciences, Kyushu University, Japan)
FT-10	TRPC6-mediated Zn^{2+} influx mitigates cardiac fibrosis through maintaining redox homeostasis Chenlin Su (Graduate School of Pharmaceutical Sciences, Kyushu University, Japan)
FT-11	Detection of Protein Tyrosine Nitration or Amination Jinwen Yang 杨劲文 (Huazhong University of Science and Technology, China)

FT-12	Discovery of small molecule inhibitors specifically targeting the Ero1α-PDI oxidative protein folding pathway Shuo Sun 孙硕 (Institute of Biophysics, Chinese Academy of Sciences, China)
FT-13	Ferrocene Correlates with Ferroptosis: Multiple Approaches to Explore Ferrocene-appended GPX4 Inhibitors as Anticancer Agents Yong Wang 王勇 (Ocean University of China, China)
FT-14	Unraveling the roles of Glutathione S-transferase P in protein S-glutathionylation modulation: Implications of therapeutic targets for oxidative organ injury Yongjie Zhang 张永杰 (China Pharmaceutical University, China)
FT-15	Loss of poly(ADP-ribose) polymerase 1 promotes catalase activation via the endothelin receptor Jiabin Yu 于佳斌 (Interdisciplinary Graduate Program in Advanced Convergence Technology & Science, Jeju National University, Korea)
FT-16	Myeloperoxidase (MPO) plays a key role in mitophagy in murine macrophages Chaorui Guo 郭朝瑞 (China Pharmaceutical University, China)
FT-17	PM2.5 induced iron accumulation-associated liver injury via activation of ferroptosis and NLRP3 inflammasome Lili Xin 信丽丽 (Soochow University, China)
FT-18	Polysulfides mediate multiple types of protein modification and tumor growth Huaiwei Liu 刘怀伟 (Shandong University, China)
FT-19	Targeting the integrated stress response and redox balance is a new strategy in meningioma inhibiting Yuanyuan Wang 王圆圆 (Institute of Biophysics, CAS, China)
FT-20	Analysis of aging biomarkers and construction of a physiological age prediction model based on cytokine profiling Lvtao Zeng 曾律滔 (Beijing hospital, China)
FT-21	Physiologically relevant Fenton-like reactions and redox cycles of labile iron species: implications for ferroptosis and Alzheimer's disease Zhongwei Zhao 赵仲伟 (Beijing University of Chemical Technology, China)
FT-22	PM2.5-induced premature senescence in HUVECs through the SIRT1/ PGC-1α/SIRT3 pathway Wu Jing 武婧 (Soochow University, China)

FT-23	The Beneficial Effects of Knockout of Astrocytic Ceruloplasmin on Learning and Memory Function in Aging Mice
	Zhongda Li 李忠达 (Ministry of Education Key Laboratory of Molecular and Cellular Biology, The Key Laboratory of Animal Physiology, Biochemistry and Molecular Biology of Hebei Province, College of Life Sciences, Hebei Normal University, China)
FT-24	The changes of genes and protein which affects mitochondrial fusion and fission in AD transgenic mice
	Seino Anna (Shibaura Institute of Technology, Japan)
FT-25	The molecular mechanism study of oxidized microRNA regulating P21 and promoting aging
	Yingmin Zhang 张英敏 (Beijing hospital, China)
FT-26	Disruption of E-prostanoid 3 receptor on cardiomyocytes protects against heart ischemia reperfusion injury
	Dong He 何东 (Shantou University Medical College, China)
FT-27	The molecular mechanism of lysosome function impairment and promotes fat accumulation by loss of G6PD
	Shanzhuang Niu 牛善壮 (Yunnan University, China)
FT-28	Endogenous hydrogen sulfide promotes the proliferation and metastasis of breast cancer through PGK1 S-sulfhydration
	Chenghua Luo 罗成华 (Medical College, Shihezi University, China)
FT-29	High PRDX4 Expression Can Predict Worse Pathological Characteristics in Cutaneous Squamous Cell Carcinom
	Jia Han 韩佳 (Department of Pathology, Kanazawa Medical University Hospital, Ishikawa, Japan)
FT-30	Hydrogen Peroxide Turn on Heat as Thermogenic agents and signals: Cellular Thermoregulation in Physiologies and Pathphysiologies
	Xu zhang 张旭 (Zhengzhou University, China)
FT-31	Increased oxidative stress induced by high-fat and high-fructose diets contribute to type 2 diabetes and its associated complications
	Qingyu Wang 王清宇 (Beijing Hospital, China)
FT-32	LPO-dependent lipid rafts inhibit immunogenic ferroptosis and pyroptosis in melanoma
	Guoquan Liu 刘国全 (Institute of Advanced Clinical Medicine, Peking University, China)

FT-33	Pharmacological targeting of NRF2 represents a promising therapeutic approach for ferroptosis-related diseases Pengfei Liu 刘朋飞 (National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, China)
FT-34	Radix Rehmanniae and its Active Ingredients Ameliorate CFA-Induced Inflammation by Attenuating Macrophage-Mediated Localized Response and Nitrative Damage Jie Chen 陈杰 (Department of Orthopedics, Shanghai Institute of Traumatology and Orthopedics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, China)
FT-35	Redox regulated Mitophagy in Arsenite-induced Malignant Transformation of Human Keratinocytes Qianlei Yang 杨乾磊 (School of Public Health, Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, MOE Key Laboratory of Geriatric Diseases and Immunology, Suzhou Medical College of Soochow University, China)
FT-36	Role of miR-3689a-3p in the regulation of mitochondrial oxidative stress in the sorafenib resistance of hepatocellular carcinoma Yau-Tuen Chan (The University of Hong Kong, China)
FT-37	S-nitrosylation enhances RhoA activity and promotes tumor cell invasion and metastasis Yusheng Lu 卢余盛 (Fujian-Taiwan-Hongkong-Macao Science and Technology Cooperation Base of Intelligent Pharmaceutics, College of Material and Chemical Engineering, Minjiang University, China)
FT-38	The circ_0071616-miR-140-3p-USP34 axis mediates FoxM1 deubiquitination in Helicobacter pylori-induced gastric malignant transformation Xize Li 李析泽 (University of Health and Rehabilitation Sciences, China)
FT-39	A Bayesian benchmark concentration analysis for urinary fluoride and intelligence in adults in Guizhou, China Tingxu Jin 金庭旭 (Suzhou Medical College of Soochow University, China)
FT-40	Circadian-Cognitive Synchrony Disrupted: Iron's Influence on Rhythmic and Memory-Related Neural Functions Qiong Wu 吴琼 (Hebei Normal University, China)
FT-41	Mechanism analysis of oxidative stress and inflammation in brain diseases Qianjin Liu 刘前进 (Xuzhou Medical University, China)
FT-42	Mechanism of arsenic regulation of mitochondrial damage and autophagy induced synaptic damage through SIRT1 and protective effect of melatonin Xiaoli Zhang 张小莉 (School of Public Health, Shanxi Medical University, China)

FT-43	Phase separation of BRD2 promotes ferritinophagy in depression Zhen Li 李振 (Shenzhen Hospital of Integrated Chinese and Western Medicine, China)
FT-44	S-nitrosoglutathione reductase alleviates morphine analgesic tolerance by restricting PKCα S-nitrosation Lingyan Su 苏凌燕 (Yunnan Agricultural University, China)
FT-45	Fecal microbe transplantation ameliorates arsenic-and-fluoride-induced nephrotoxicity of offspring rats co-exposure to arsenic and fluoride through microbiota-gut-kidney axis Xiaolin Tian 田晓琳 (Shanxi Medical University, China)
FT-46	Metabolic reprogramming in placental mitochondria respiration contributes to the reproductive success of indigenous Tibetan women living at high altitude Jicuomao Niang 娘吉措毛 (Affiliated Hospital of Qinghai University (School of Clinical Medicine), China)
FT-47	Ganoderma Lucidum Spore Lehuo Powder Attenuates Experimental Autoimmune Encephalomyelitis by Modulating Microglial Activation and Polarization through the NF-κB Signaling Pathway Lu Zhang (School of Chinese Medicine, LKS Faculty of Medicine, the University of Hong Kong, China)
FT-48	Brain-targeted liposomes with neuroprotective effects for precise therapy of ischemic stroke Siyu Tian 田丝雨 (Hebei Normal University, China)
FT-49	Inorganic Nanosensitizers for Cancer Nanodynamic Therapy Xiaoyan Zhong 仲晓燕 (Soochow University, China)
FT-50	Nano-assemblies overcome cancer multidrug resistance for effectively synergistic chemo-immuno-oncotherapy Yingnan Liu 刘英楠 (University of Salzburg, China)
FT-51	Nanomaterials for tumor-cell-specific catalytic therapy Xi Hu 胡希 (Anhui University of Chinese Medicine, China)
FT-52	Nanomedicine by Modulating ROS for Oncotherapy Guofang Zhang 张国芳 (Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China)
FT-53	Protective effect of platinum nano-antioxidant and nitric oxide against hepatic ischemia-reperfusion injury Jing Mu 穆婧 (Peking University Shenzhen Hospital, China)

FT-54	Disruption of circadian rhythms promotes ventricular arrhythmia via oxidative stress and electrocardiography alternation Bingping Yang 杨冰萍 (Shantou University Medical College, China)
FT-55	Chrysanthemolide J mitigates acetaminophen-induced hepatotoxicity through LKB1 and PP2A-mediated mitochondrial hormesis Fei Zhou 周飞 (University of Macau, China)
FT-56	Network Medicine landscape on the Health-Enhancing Properties of Natural Antioxidants Mengchen Liu 刘梦晨 (Zhuhai Campus of Zunyi Medical University, China)
FT-57	Osteoprotective and osteoblastic potential of the Sambucus javanica Reinw ex Blume subsp. javanica leave Treethip Sukkho (Department of Biotechnology, Multidisciplinary and Interdisciplinary School, Chiang Mai University, Chiang Mai, Thailand)
Venue: The Ballroom A	
PO-01	A New Approach for Treatment of Atopic Dermatitis: Plasma-activated Solutions Tingyi Yin 殷婷怡 (The First Affiliated Hospital of Xi'an Jiaotong University, China)
PO-02	An assessment of Redox-stress Response Capacity (RRC) Shilong Li 李世龙 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-03	Construction of the platform for precision redox detection and regulation Minghao Deng 邓明昊 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-04	Effect of electrolytic water generated by an alkaline ionizer on the concentration change of kelp extract Sato Takuma (Shibaura Institute of Technology, Japan)
PO-05	Exploring the Precision Redox Map of Cells and *C. elegans* under Different Treatment Conditions with High Glucose Yuyunfei Huang 黄雨云飞 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-06	Improvement of mouse bone marrow transplantation and chimerism analysis by qPCR of the modified gene Gang Yu 余钢 (Shantou University Medical College, China)
PO-07	One-step ligation of the phosphine-thioester elucidates the landscape of S-nitrosation proteome in lipopolysaccharide-related inflammation Hui Ye 叶辉 (China Pharmaceutical University, China)

PO-08	Trityl-based biradical as EPR probe for superoxide radical with enhanced sensitivity Yurui Leng 冷雨睿 (Tianjin Medical University, China)
PO-09	Browning effect of Inguinal White Adipose Tissue by a Novel Lignan (-)-Secoisolariciresinol 4-O-Methyl Ether, Modified from Arctigenin, Attenuates Diet-induced Obesity by Activating Mitochondria and Peroxisomes Wenjun Jiao (Department of Science in Korean Medicine, Graduate School, Kyung Hee University, Korea)
PO-10	CPD84: A Novel PPI inhibitor Targeting ELF3-PtnA Interaction to Modulate Angiogenesis in Ovarian cancer Moon Inhye (Ewha Womans University, Korea)
PO-11	Development of Nitric Oxide-Donating Netarsudil Derivatives as a Synergistic Therapy for Glaucoma with Reduced Ocular Irritation Cunrui Li 李存睿 (China Pharmaceutical University, China)
PO-12	Development of novel trityl radicals as efficient buffers for superoxide radical via unprecedented reversible reactions Longfei Gao 高龙飞 (School of Pharmacy, Tianjin Medical University, China)
PO-13	Discovery of Selective Cathepsin S Inhibitors as Potential Therapeutic Agents for Triple-Negative Breast Cancer Liu Yi (Ewha Womans University, Korea)
PO-14	Genome-wide CRISPR Screening of Genes Regulating Endoplasmic Reticulum H_2O_2 Qiaoli Zhu 朱乔丽 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-15	GTSE1 promotes pulmonary fibrosis through the induction of EMT Jin Hee (Graduate School of Pharmaceutical Sciences, Ewha Womans University, Korea)
PO-16	In Situ Generation and High Bioresistance of Trityl-based Semiquinone Methide Radicals under Anaerobic Conditions in Cellular Systems Xizi Du 杜习姿 (Tianjin Medical University, China)
PO-17	MS-based Exclusive Isolation Study Unveils a Novel Anti-Melanogenic Phenolic Glycoside from Idesia Polycarpa Maxim Jung-Eun Lee (Dongguk University, Korea)
PO-18	Optimization for Bioactive Compounds, Antioxidant Activity of Complex Extract Containing Three Herbs Grown in Korea Using a Simplex-Centroid Mixture Design Jeoung-Gyu Lee (Hanyang University, Korea)

PO-19	Protective roles of supersulfides on acetaminophen induced liver injury Chunyu Guo (Kumamoto University, Japan)
PO-20	Single-Cell Analysis Reveals Cell-Specific Patterns and Spatiotemporal Regulation of Nuclear Redox State Miaoling Yang 杨淼泠 (Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, China)
PO-21	Supersulfides protect against SARS-CoV-2 infection via suppression of the viral thiol proteases Jia Yao (Department of Environmental Medicine and Molecular Toxicology, Tohoku University Graduate School of Medicine, Japan)
PO-22	The function of sulfite oxidase in mitochondrial supersulfide metabolism Yingchi Xia 夏应驰 (Tohoku University, Japan)
PO-23	TRPC3-Nox2 complex formation participates in the progression of striated muscle atrophy Di Wu (Department of Physiology, Graduate School of Pharmaceutical Sciences, Kyushu University，Japan)
PO-24	Blockade of the TP Receptor Ameliorates the Ischemic Renal Disorders in PGIS Deficient Mice Jiahui Ge 葛佳辉 (Shantou University, China)
PO-25	Effect and mechanism of oligodendrocyte knockout of Fpn1 in mice on depression-like behavior Na Zhang 张娜 (Hebei Normal University, China)
PO-26	Hydrogen Sulfide Targets S-Sulfhydrated-cAMP-response element binding protein (CREB) Cys286 Residues to Inhibit the epithelial-mesenchymal transition (EMT) in Chronic Renal Injury Shuai Chen 陈帅 (Capital Medical University, China)
PO-27	Impact of tyrosine amination on the aggregation and neurotoxicity of amyloid-β: Unveiling a potential defensive mechanism in Alzheimer's disease Ting Hu 胡婷 (Huazhong University of Science and Technology, China)
PO-28	Insufficient S-sulfhydration of serum and glucocorticoid-regulated kinase 1 participates in hyperhomocysteinemia-induced liver injury Xinyu Zhu 祝新宇 (Capital Medical University, China)
PO-29	Near-infrared fluorescent probes for imaging vimentin in the brain of ischaemic stroke mice Simiao Zhang 张思淼 (Shandong Normal University, China)
PO-30	Prostaglandin E2 promotes platelet aggregation and thrombogenesis via Thromboxane A2 receptor besides its canonic receptor EP3 Kaiqi Xie 谢恺麒 (Medical College of Shantou University, China)

PO-31	Redox-inducible Radiomimetic Photosensitizers Selectively Suppress Cancer Cell Proliferation by Damaging DNA through Radical Cation Chemistry Luo Wang 王洛 (Tianjin Medical University, China)
PO-32	S-nitrosation of CaMKIIα matters, a new mechanism mediating learning and memory Boyu Chu 褚博煜 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-33	The effect of water-soluble metalloporphyrin FeTPPS on membrane damage and cytotoxicity induced by hIAPP Zhilong Wang 王智龙 (Huazhong University of Science and Technology, China)
PO-34	The S-nitrosation of CKMT1 impedes intracellular energy shuttling by inducing its dissociation from octamer to dimer Tiepeng Wang 王铁鹏 (The Institute of Biophysics, Chinese Academy of sciences, China)
PO-35	Screenings of nanoantibodies against protein disulfide isomerase and its antiplatelet aggregation effects Guozhen Cui 崔国祯 (School of Bioengineering, Zhuhai Campus of Zunyi Medical University, China)
PO-36	Analysis of the translation stalling sensor protein GCN1 complex using the proximity-dependent biotinylation enzyme TurboID Kazuki Hasegawa (Hirosaki University Graduate School of Medicine, Japan)
PO-37	Carbon dots cause developmental toxicity in zebrafish embryos via endoplasmic reticulum stress-mediated lipid dysregulation Zeng Liwen 曾丽雯 (Soochow University, China)
PO-38	Ceruloplasmin deficiency in Leydig cells causes testicular dysfunction via iron-mediated oxidative stress in mice Lihui Wu 吴丽辉 (Hebei Normal University, China)
PO-39	Domperidone induces apoptosis via inactivation of β-arrestin2-dependent MEK/ERK/STAT3 pathway in of human colon cancer cells So Jin Sim (Keimyung University, Korea)
PO-40	Environmental toxin exposure-induced oxidative stress impairs chromosome cohesion and segregation in mammalian oocytes Yan Yun 云彦 (Shantou Central Hospital, China)
PO-41	Karyoptosis is a cyclic AMP-responsive element binding protein 3 driven novel regulated cell death Weidong Chen (The Catholic University of Korea, Korea)

PO-42	Loss of poly(ADP-ribose) polymerase 1 boosts catalase activation via endothelin receptors Jiabin Yu (Interdisciplinary Graduate Program in Advanced Convergence Technology & Science, Jeju National University, Korea)
PO-43	Myriocin regulates cellular redox homeostasis via mitochondrial hormesis Wenling Gu 顾文凌 (Key Laboratory of Bio-Resources and Eco-Environment of Ministry of Education, College of Life Science, Sichuan University, China)
Venue: The Ballroom C	
PO-44	Protective Effects of OM2 Plant Extract against Oxidative Stress and Inflammation in Arsenic Exposed RAW264.7 cells Hyejin Kim (Hanyang University, Korea)
PO-45	The effects of local iron treatment on intervertebral disc degeneration Chenchen Li 李晨晨 (Hebei Normal University, China)
PO-46	The Function of 2-Mercaptoethanol in the Repair of DNA during Kidney Ischemia and Reperfusion through GPX4 Upregulation Moon Daeun (Department of Anatomy, Jeju National University College of Medicine, Korea)
PO-47	The Role and Mechanisms of Prostaglandin E2 Receptor EP3 in Acute Lung Injury Zhengpeng Zeng 曾征鹏 (Shantou University Medical College, China)
PO-48	Water-soluble single molecular probe for simultaneous detection of viscosity and hydrazine Jiazi Yin 尹佳子 (Guangdong University of Petrochemical Technology, China)
PO-49	Assessing Myriocin and NAC for protection against cisplatin induced hearing loss and renal toxicity in Mice Zhiyi Liu 刘治义 (The College of Life Science, Sichuan University, China)
PO-50	Dimethyl α-Ketoglutarate Promotes the Synthesis of Collagen and Inhibits Metalloproteinases in HaCaT Cells Bo-Yeong Yu (Dongguk University, Korea)
PO-51	Dynamic proteostasis imbalance is a hallmark of aging Chang Shi 时畅 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-52	Increasing redox-stress signaling threshold (RST) through stress to delay aging Haoyang Shi 时浩洋 (Institute of Biophysics, Chinese Academy of Sciences, China)

PO-53	Inhibition of ER Stress as a Protective Strategy of 3, 3', 4', 5, 5', 7 Hexahydroxyflavone against PM2.5-induced Apoptosis in Skin Cells Herath Mudiyanselage Udari Lakmini Herath (Department of Biochemistry, College of Medicine, and Jeju Research Center for Natural Medicine, Jeju National University, Korea)
PO-54	Optimization of Brain Microvascular Endothelial Cell Extraction Ruikun Xie 谢睿坤 (Hebei Normal University, China)
PO-55	Quercetin 3-D-galactoside mitigates PM2.5-mediated keratinocyte cell senescence by alleviating the endoplasmic reticulum and mitochondrial stress Pincha Devage Sameera Madushan Fernando (Department of Biochemistry, College of Medicine, and Jeju Research Center for Natural Medicine, Jeju National University, Korea)
PO-56	Relationship between ferroptosis and cellular senescence caused by particulate matter 2.5 in skin keratinocytes Meijing Piao (Department of Biochemistry, College of Medicine, and Jeju Research Center for Natural Medicine, Jeju National University, Korea)
PO-57	The modification of 8-oxyguanine in the microRNA seed region regulates aging process Jiaqi Guo 郭佳琪 (Beijing Hospital, China)
PO-58	Txn1-F54L mutation in rats generates neurodegeneration and chronic kidney disease through mitochondrial dysfunction and multiple cell death modes Iori Ohmori (Faculty of Education, Department of Child Neurology, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Japan)
PO-59	Chemerin Activates the NLRP3 Inflammasome Through CMKLR1, Mediating Potassium Current Dysregulation and Obesity-Related Atrial Fibrillation Yating Chen 陈雅婷 (Medical School of Chinese PLA, China)
PO-60	Different roles of E-prostanoid 3 receptor on renal parenchymal cells and myeloid cells in acute oxalate nephropathy Jinwei Guo 郭锦伟 (Shantou University Medical College, China)
PO-61	Dysregulated peroxisomal metabolites in cardiac adipose tissue induce heart dysfunction Se Jin Jung (Department of Science in Korean Medicine, Graduate School, Kyung Hee University, Korea)
PO-62	GSNOR contributes to age-related obesity by regulating the S-nitrosation of Beclin-1 to promote adipose tissue whitening Ting Xie 谢婷 (Institute of Biophysics, Chinese Academy of Sciences, China)

PO-63	Hepatic Adenosine Kinase mitigates hepatic steatosis and insulin resistance in obese mice Kai Luo 骆开 (College of Life Sciences, University of Chinese Academy of Sciences, China)
PO-64	Inhibition of GCN2 alleviates hepatic steatosis and oxidative stress in alcoholic-related liver disease Ying Xu 徐颖 (University Network Teaching Platform, University of Chinese Academy of Sciences, China)
PO-65	Intestinal flora-bile acid-FXR axis regulates hepatic lipid metabolism induced by arsenic and fluoride co-exposure in rats Jinyao Chen 陈锦瑶 (Shanxi Medical University, China)
PO-66	Knocking out GCN2 exacerbates oxidative stress in the liver under zinc-deficient conditions by reducing Nrf2 expression Zhuoran Yu 于卓然 (University of Chinese Academy of Sciences, China)
PO-67	Machine learning based model for predicting coronary heart disease using dynamic triglyceride-glucose index: a Longitudinal study cohort CHARLS database Yi Yang 杨易 (I.T. Department of Faculty of Engineering and Information Technology of university of technology Sydney, Australia)
PO-68	Nfe2l1 deficiency exacerbates alcohol-induced liver injury in mice Jinghui Qu 曲景辉 (China Medical University, China)
PO-69	Obesity-induced Nox2 activation prolongs cardiac repolarization Bin Li 李彬 (The Eighth Medical Center of PLA General Hospital, China)
PO-70	Paeonol Induces Thermogenesis by Suppressing Endoplasmic Reticulum Stress via NRF2 Activation in Beige Adipocytes Ja Yeon Park (Department of Science in Korean Medicine, Graduate School, Kyung Hee University, Seoul, Korea)
PO-71	Suppression of O-GlcNAc transferase (OGT) inhibits adipogenesis in 3T3-L1 adipocytes through the modulation of PPARγ O-GlcNAcylation Hoang Hai Ngo (Dongguk University, Korea)
PO-72	YY1 nitration participates in T2DM induced-cardiomyocyte lipotoxicity by inhibiting Anxa3 transcription Jiayin Chai 柴嘉音 (Capital Medical University, China)
PO-73	α-Ketoglutarate pretreatment prevents hyperlipidemia-induced endothelial injury and fatty liver by ameliorating mitochondrial dysfunction and oxidative stress Danyu Cheng 程丹雨 (Xi'an Jiaotong University, China)

PO-74	A fluorescence-enhanced near-infrared fluorescent probe for real-time imaging of protein sulfenic acids in oxidative stress
	Zhixuan Feng 冯芷璇 (Institute of Chemistry, Chinese Academy of Sciences, China)
PO-75	Acute lung injury induced by acid aspiration or lipopolysaccharide leads to liver injury and hepatic regulated cell death in mice
	Cheng Peng 彭程 (Cardiovascular Research Center, Shantou University Medical College, China)
PO-76	COX7A1 heightens the susceptibility of human NSCLC cells to cystine deprivation-induced ferroptosis
	Rongrong Liu 刘蓉蓉 (The Second Affiliated Hospital of Xi'an Jiaotong University, China)
PO-77	Decomposable Nanodrugs Inducing Immunogenic Cell Death and cGAS-STING Pathway Activation for Enhanced Photodynamic Chemotherapy-Driven Immunotherapy
	Chenchen Li 李晨晨 (Hebei North University, China)
PO-78	Dehydrocostus lactone as a potential therapeutic agent for colorectal cancer and dextran sulfate sodium-induced colitis in mice
	Sun-Young Hwang (College of Korean Medicine, Dongshin University, Korea)
PO-79	Europium-modified carbon nitride nanosheets for smartphone-based fluorescence sensitive recognition of anthrax biomarker dipicolinic acid
	Wenhao Du 杜文浩 (Guangdong University of Petrochemical Technology, Korea)
PO-80	Exploring immune evasion mechanism mediated by superoxide anion of hepatic stellate cells by fluorescence imaging
	Yuantao Mao 毛元涛 (Shandong Normal University, China)
PO-81	Exploring Nitroproteomics in Cancer Biology: A Case Study of Early Onset Gastric Cancer
	Kwang Pyo Kim (Kyung Hee University, Korea)
PO-82	Hepatic Sinusoidal Endothelial Cells Targeted Delivery of Nitric Oxide via Glycosyl-modified Glycosidase to Treat Liver Fibrosis
	Jingjie Tan 谭靖节 (Tianjin Medical University, Tianjin, China)
PO-83	Investigating the Relationship Between Tumor Stem Cells, Oxidative Stress, and Cisplatin Resistance in Ovarian Cancer
	Jinzhi Lu 鲁锦志 (The First Affiliated Hospital of Yangtze University, China)
PO-84	Liposomes-encapsulated hERG Potassium Channel Probe for Glioblastoma Therapy and Imaging
	Li Liu 刘丽 (Shandong Normal University, China)

PO-85	Manipulating disulfide bond formation of the Spike protein to inhibit the SARS-CoV-2 infection Xinqian Li 李欣倩 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-86	New approach to tumor therapy: Targeting the destruction of redox balance Qiwen Luo 罗其文 (Key Laboratory of Metabolism and Molecular Medicine of the Ministry of Education, Department of Biochemistry and Molecular Biology, School of Basic Medical Sciences, Fudan University, China)
PO-87	Repurposing Flubendazole for Glioblastoma Ferroptosis by Affecting xCT and TFRC Proteins Wei Teng 滕炜 (Guizhou Medical University, China)
PO-88	Respiratory exposure to lithium nickel manganese cobalt oxide particles induces multi-organ damage and disrupts redox homeostasis in mice Junyi Wang 王君仪 (China Medical University, China)
PO-89	Role and mechanism of nanomedicine with ROS regulating ability for differentiation therapy of myeloid neoplasia Haiyan Xu 许海燕 (Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences & Peking Union Medical College, China)
PO-90	Synthesis and study of β-glucuronidase controlled fluorescent probe Anqi Li 李安琪 (Tianjin Medical University, China)
PO-91	The acceleration of iron transport promotes the malignancy of glioma through Oxidizing 293 cysteine on sirt5 by the increased production of H_2O_2 Fei Wang 王飞 (Hebei Normal University, China)
PO-92	β-Lapachone Enhances NETosis through Reactive Oxygen Species Generation: Mechanistic Insight in Neutrophil-Mediated Innate Immunity Jisoo Han (Department of Science in Korean Medicine, Graduate School, Kyung Hee University, Korea)
PO-93	A Versatile Fluorescent Probe for Hydrogen Peroxide in Serotonergic Neurons of Living Mouse Brains with Depression Feida Che 车飞达 (School of Chemistry, Chemical Engineering and Materials Science, Shandong Normal University, China)
PO-94	DDAH1 attenuates MPTP-induced Parkinson's disease impairment via FOXO3 mediated signals Zhirui Li 李祉睿 (Capital Medical University, China)

PO-95	Discovery of potent LRRK2 inhibitors by ensemble virtual screening strategy and bioactivity evaluation
	Shuli Li 李淑黎 (University of Macau, China)
PO-96	Environmental standard limit concentration' arsenic exposure is associated with anxiety, depression, and autism-like changes in early-life stage zebrafish
	Yuanhui Zhu 朱原慧 (Department of Toxicology, School of Public Health, Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, China)
PO-97	Exploring the Neuroinflammatory Pathways of 8-oxoGTP and Their Effects on Cognitive Decline
	Jin Li 李瑾 (Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, China)
PO-98	Functional study of TMPRSS6 in APP/PS1 mouse
	Hongtao Sun 孙洪涛 (HeBei Normal University, China)
PO-99	GSNOR, a new player in depression
	Chuanxin Sun 孙传鑫 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-100	Hydrogen peroxide in midbrain sleep neurons regulates sleep homeostasis
	Yujing Tian 田玉静 (Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences, China)
PO-101	Improving mitochondrial function with arachidonic acid supplementation to alleviate cognitive deficits in schizophrenia patients
	Yan Gao 高琰 (Shanghai Jiao Tong University, Bio-X Institutes, China)
PO-102	Melatonin derivative 6a protects Caenorhabditis elegans from formaldehyde neurotoxicity via ADH5
	Na Feng 冯娜 (School of Pharmacy and Food Engineering, Wuyi university, China)
PO-103	Nos2b regulates injury-induced cxcl18b-defined transitional state Müller Glia proliferation in the zebrafish retina
	Aojun Ye 叶傲君 (Institute of Biophysics, Chinese Academy of Sciences, China)
PO-104	Overexpressed of ferrous iron ions triggers Neutrophil extracellular trap formation and contributes to multiple sclerosis
	Shenyu Yan 颜深玉 (The University of Hong Kong, China)
PO-105	Oxidative stress increased β-galactosidase activity in the brains of mice with depression
	Deqiang Li 李德强 (Institutes of Biomedical Sciences, Shandong Normal University, China)

PO-106	Perturbation in mitochondrial quality control is associated with oxidative mitochondrial damage in patients with schizophrenia Shuhui Li 李书慧 (Shanghai Jiao Tong University, China)
PO-107	Pyran compounds 7r reduces α-synuclein aggregation and protects neuronal activity in Caenorhabditis elegans by modulating the oxidative stress pathway and enhancing the activation of autophagy Ruiting Han 韩瑞婷 (Wuyi University, China)
PO-108	Restoring the redox and norepinephrine homoeostasis in mouse brains promotes an antidepressant response Qi Ding 丁琪 (Shandong Normal University, China)
PO-109	Sodium Danshensu Attenuates Blood-Brain Barrier Disruption and Hemorrhagic Transformation in Ischemic Stroke Rats with Acute Hyperglycemia: Involvement of ONOO-NLRP3 Inflammasome Pathway Shuang Chen 陈霜 (The University of Hong Kong, China)
PO-110	Superoxide anion-mediated mitochondrial dysfunction in the hippocampus of depressed mice revealed by fluorescent sensing and labeling strategies based on tandem activity Xiwei Li 李玺威 (Shandong Normal University, China)
PO-111	Synergistic effects of Tanshinone IIA sustained release nano particles on Parkinson's disease insults Yuhao Kan 阚宇豪 (Capital Medical University, China)
PO-112	TFR Enhances α-Synuclein-mediated Ferroptosis in the Hippocampus of Parkinson's Disease Dementia Lijun Zhao 赵丽君 (Shenzhen Hospital of Integrated Traditional Chinese and Western Medicine, China)
PO-113	The beneficial effect of Angong Niuhuang Pill (AGNHP) on ischemic stroke via the regulation of gut microbiota Ao Shang 商奥 (The University of Hong Kong, China)
PO-114	The Deubiquitination of Erg1 by USP7 Regulates Nrf2 Redox Balance and Mitigates Fluoride-Induced Neurotoxicity Wenjin Qiu 仇文进 (The Affiliated Hospital of Guizhou Medical University, China)
PO-115	The effect and mechanism of knockdown Ferroportin1 in microglia on cerebral ischemia-reperfusion injury Qiaoya Zhao 赵悄雅 (The Laboratory of Iron Metabolism, College of Life Science, Hebei Normal University, China)

PO-116	Synthesis and characterization of Tanshinone IIA nanoparticles for the treatment of cerebral stroke Sihan Wang 王思涵 (Department of Pharmacology, School of Basic Medical Sciences, Capital Medical University, China)
PO-117	Fluorescence-enhanced detection of hypochlorite based on in situ synthesis of functionalization-free carbon spheres Tianhong Liu 刘天鸿 (Guangdong University of Petrochemical Technology, China)
PO-118	Liver injury induced by subchronic respiratory exposure to lithium nickel cobalt manganese oxide in mice Yongqin Xia 夏永钦 (China Medical University, China)
PO-119	Preparation of baicalin self-microemulsified preparation and study on its radiation protection effect Xinran Liu 刘欣然 (Huazhong University of Science and Technology, China)
PO-120	Biyuantong decoction reduces postoperative recurrence of chronic rhinosinusitis by inhibiting ferroptosis Yinyin Yao 姚茵茵 (Fujian University of Traditional Chinese Medicine, China)
PO-121	Coptisine Reduces Transformation Process From Chronic Atrophic Gastritis to Gastric Cancer via Inhibiting Hepcidin Expression Yashuo Zhao 赵亚硕 (Hebei University of Chinese Medicine, China)
PO-122	Dihydroisotanshinone I functions as an agonist of TRPV1 to alleviate lipopolysaccharide-induced neuroinflammation in vitro and in vivo Nan Xu 徐楠 (University of Macau, China)
PO-123	RSM for Revealing Traditional Chinese Medicine's Yun Qi Wisdom Based on the Theory of Superstrings Jiulong Chen 陈久龙 (Dahua Group Co., Ltd., China)
PO-124	A phosphatase-like nanomaterial promotes autophagy and reprograms macrophages for cancer immunotherapy Su Li 李苏 (Laboratory of Immunology and Nanomedicine, Laboratory of Inflammation and Vaccines, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China)
PO-125	In situ nitric oxide production for selective S-nitrosation as a promising synergistic cancer treatment strategy Chen Zhang 张宸 (China Pharmaceutical University, China)
PO-126	liver-targeted plasmid lipid nanomedicine treats liver fibrosis by ROS elimination Zhengxun Liu 刘正汛 (Hebei Normal University, China)

PO-127	NOS-like activity of CeO_2 nanozymes contributes to diminishing the vascular plaques Yuxiang Sun 孙玉祥 (Yangzhou University, China)
PO-128	Therapeutic effect of PN-CeO_2 on atopic dermatitis by regulating oxidative stress in keratinocytes and macrophages Ruimin Bai 白瑞敏 (Department of Dermatology, The First Affiliated Hospital of Xi'an Jiaotong University, China)
PO-129	A Catechol Isoquinoline Salsolinol Induces Apoptosis of Human Liver Cancer Cells by Regulating the STAT1/3 Signaling Jeong-Hwa Woo (Basic Science Research Institute, Sungshin Women's University, Korea)
PO-130	Acute Sleep Deprivation Induces Liver Damage and Protective Effects of Chalcone Analogue TAK Yifang Wang 王一方 (Xi'an Jiaotong University, China)
PO-131	Assessing Myriocin and N-Acetyl Cysteine on Age-Related Hearing Loss and disruption of Advanced Glycation End Products in mice Lin Cheng 程琳 (State Key Laboratory of Biotherapy, Sichuan University, China)
PO-132	Characterization of a polysaccharide from Amauroderma rugosum and its proangiogenic activities in vitro and in vivo Xin Nie聂欣 (University of Macau, China)
PO-133	Co-Treatments of Gardeniae Fructus and Silymarin Ameliorates Excessive Oxidative Stress-Driven Liver Fibrosis by Regulation of Hepatic Sirtuin1 Activities Using Thioacetamide-Induced Mice Model Jin A Lee (Daegu Haany University, Korea)
PO-134	Daphnetin ameliorates hepatic steatosis by suppressing peroxisome proliferator-activated receptor gamma (PPARG) in ob/ob mice Zhen Wang 王珍 (Xi'an Jiaotong University, China)
PO-135	Emodin, a major component of Cassia seed extract, exhibits potent anti-inflammatory effects in vitro and in vivo Kwanhwan Wi (College of Korean Medicine, Dongshin University, Korea)
PO-136	Exploring the Mechanisms of Action of Active Constituents in Schisandrae Fructus for the Management of Diabetic Cardiomyopathy Jihang Chen 陈吉航 (The Chinese University of Hong Kong, Shenzhen, China)
PO-137	Ferulic acid as a potent natural antioxidant: mechanisms and applications in animal health and production Yongquan Han 韩永权 (Guangzhou Cohoo Biotechnology Co., Ltd., China)

PO-138	Gaudichaudione H ameliorates liver fibrosis and inflammation by targeting NRF2 signaling pathway Mengjiao Shi 石梦姣 (National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, China)
PO-139	Neem leaf extract exhibits anti-aging and antioxidant effects from yeast to human cells Jinye Dang 党劲野 (Sichuan University, China)
PO-140	Saikosaponin A suppresses inflammation in DSS-induced colitis mouse model Young-Gwon Kim (College of Korean Medicine, Dongshin University, Naju, Korea)
PO-141	Salsolinol Alleviates Tumor Formation and Anxiety Like Behaviors in the Diethyl Nitrosamine-induced Hepatocarcinogenesis in Mice Chan-Mi Park (Department of Future Applied Sciences, College of Natural Sciences, Sungshin Women's University, Korea)
PO -142	The ROMO1-LONP1-SIRT3 axis protects against hepatic steatosis via promoting mitochondrial lipid catabolism Kun Peng (Institute of Molecular Medicine, College of Future Technology, Peking-Tsinghua Center for Life Sciences, Peking University, China)
PO-143	Dexmedetomidine's Protective Effects and Mechanisms on Lung Injury Induced by Vesicant Sulfur Mustard SHI Minjie 师敏婕 (Air Force Medical University, China)
PO-144	Glutathione-sensitive mesoporous nanoparticles loaded with cinnamaldehyde for chemodynamic and immunological therapy of cancer Lichong Zhu 祝李冲 (National Engineering Research Center for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, China)
PO-145	Hyperbaric oxygen augments probiotic-derived selenium nanoparticles-induced oxidative stress to enhance cancer immune checkpoint blockade therapy Puze Li 李璞泽 (National Engineering Research Center for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, China)
PO-146	Engineered Extracellular Vesicles to Enhance Antigen Presentation for Boosting Light-Driven Tumor Immunotherapy Xuyu Li 李旭钰 (National Engineering Research Center for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, China)
PO-147	Leveraging tumor-repopulating cell-derived microparticles for enhanced cancer therapy via targeted Akkermansia muciniphila modulation chemotherapy Shiyu Li 李诗雨 (National Engineering Research Center for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, China)

PO-148	DNA-functionalized extracellular vesicles for efficient free radical prodrug activation in cancer therapy Zhiheng Cai 蔡之恒 (National Engineering Research Center for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, China)
PO-149	Targeted intervention in nerve-cancer crosstalk enhances pancreatic cancer chemotherapy Jingjie Liu 刘婧杰 (National Engineering Research Center for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, China)
PO-150	Glutaminolysis inhibition sensitizes cuproptosis by regulating oxidative stress to eliminate cancer stem cells Zitao Fan 樊子涛 (College of Life Sciences and Technology, Huazhong University of Science and Technology, China)

Design, synthesis and antiparasitic activity of a novel naphthoquinone molecule based on SjTGR from Schistosoma Japonicum

Yan Wang（王炎）, Hui Gao, Xiaoli Tan, Yuguang Song* and Yangping Liu**

Tianjin Key Laboratory on Technologies Enabling Development of Clinical Therapeutics and Diagnostics, School of Pharmacy, Tianjin Medical University, Tianjin 300070.

**Correspondence email: wy15230291987@163.com.*

Abstract

Copper is an essential micronutrient for all organisms and often serves as a catalytic/structural component for protein. Copper ions also catalyze the production of reactive oxygen species, leading to oxidative stress and subsequent cellular damage. Dysregulation of copper homeostasis is closely associated with various diseases including cancer, neurodegenerative diseases, Menkes and Wilson's diseases. Therefore, precise detection and quantitation of copper ions is essential for deep understanding into its pathophysiological roles. However, current detection techniques for copper ions have still been limited by their invasiveness, poor specificity, low sensitivity or failure with dynamic monitoring. In this study, we report a new EPR approach for highly specific and sensitive detection of the diamagnetic Cu(I) via its hyperfine splitting interaction with the cyclen-linked trityl probe TCuP1. TCuP1 formed a stable 1:1 complex with Cu(I) which exhibited a characteristic EPR four-line signal due to Cu(I) (I = 3/2 for both 63Cu and 65Cu). The fingerprint signal together with specific recognition of the cyclen moiety to Cu(I) endowed TCuP1 with high specificity to Cu(I), thus enabling quantitative detection of Cu(I) from a mixed sample of 14 metal ions and dynamic monitoring of the Cu(II)/Cu(I) redox cycle. TCuP1 was highly sensitive to Cu(I) with a detection limit of 10 nM. This work paves a way for detection of diamagnetic metal ions with non-zero nuclear spins by EPR.

Deciphering the RSS code in cellular senescence

Nai-Kei Wong

Shantou University Medical College

**Correspondence email: wongnk@stu.edu.cn*

Abstract

ROS/RNS (reactive oxygen/nitrogen species), lipid free radicals and other reactive metabolic intermediates have been recognized as pivotal drivers of cellular senescence and organismal aging, though relatively little is known about RSS (reactive sulfur species), in particular, the gaseous molecule hydrogen sulfide (H2S), as a mediator in the redox landscape of aging. H2S confers pleiotropic benefits on multiple aspects of the aging juggernaut including telomere attribution, mitochondrial dysfunction, genomic instability, and loss of proteostasis. Dietary organosulfur compounds such as lipoic acid (LA) constitute a rich and accessible source of biologically assimilable sulfur-containing intermediates that can be tapped as a potential resource for anti-aging applications. The mechanisms underlying LA's observed senolytic potential, however, remain to be clarified. Herein, we venture to develop a series of selective and photostable fluorescent probes (SulfurRed-1) for H2S detection, and use them to characterize pharmacological effects of LA derivatives targeting cellular organelles. Our current results suggest that H2S generation is dynamically coupled to that of ROS, and that LA derivatives can effectively mitigate oxidative stress in contexts of cellular senescence, ferroptotic cell death and beyond.

Detection and evaluation of novel oxidizing substances in sodium hypochlorite using Trolox

Ayuta Kishimoto[1], Yuta Okada[2], Kenta Sugiyama[2], Masahiro Kohno[2], Koji Fukui[1,2].

[1] Functional Control Systems, Graduate School of Engineering and Science, Shibaura Institute of Technology.
[2] Systems Engineering and Science Graduate School of Engineering and Science, Shibaura Institute of Technology.

**Correspondence email: mf22045@shibaura-it.ac.jp*

Abstract

The COVID-19 pandemic has heightened interest in disinfection and sterilization practices in daily life. Among them, chlorine-based disinfectants have gained attention as an alternative to alcohol-based disinfectants. These disinfectants are thought to be effective against a wider range of microorganisms than alcohol-based disinfectants due to the oxidizing power of hypochlorous acid and hypochlorite ions. There are primary components of chlorine-based disinfectants. It is known that the oxidizing power of hypochlorous acid and hypochlorite ions changes depending on the pH, due to the pH dissociation properties of sodium hypochlorite. Sodium hypochlorite is typically alkaline and exists mostly as hypochlorite ions. It is thought that when the pH becomes acidic, hypochlorite ions are converted into hypochlorous acid and chlorine gas. While it is established that hypochlorite ions, hypochlorous acid, and chlorine gas all possess oxidizing power and contribute to disinfection, the exact sterilization mechanisms of these substances remain unclear. This purpose of this study was to reanalyze sodium hypochlorite solutions using spectrophotometry, pH measurements, ion chromatography, and electron spin resonance. To evaluate the oxidative potential, we added Trolox, a vitamin E antioxidant, to sodium hypochlorite solution. The results showed that the hypochlorite ions in the sodium hypochlorite solution do not have oxidizing power, indicating that there may be other substances present. We report these findings and discuss their implications for understanding the sterilization mechanism of sodium hypochlorite.

Key Words: Sodium hypochlorite; Radical; Oxidative stress

High sensitive LC-MS/MS method for determining malondialdehyde in biological sample using thiobarbituric derivatization

Ujihara Miyu

Kyoto University

**Correspondence email: ujihara.miyu.43c@st.kyoto-u.ac.jp*

Abstract

Malondialdehyde (MDA) is a secondary product from lipid peroxide in food and body and has been quantified in numerous studies as an indicator of oxidative stress in the body. Reaction of MDA with 2-thiobarbituric acid (TBA) generates red color thiobarbituric acid reactive substances (TBARS). Thus, MDA is widely quantified by measuring absorbance at 515 nm following conversion to TBARS. However, in addition to MDA, TBA also reacts with various aldehydes and protein degradation products, and it has been suggested that some of them and byproducts exhibit red color. Generation of these red substance can interfere determination of MDA by the conventional colorimetric TBARS method. Thus, some HPLC and LC-MS/MS methods for determination of MDA using TBA derivatization have been introduced. However, these methods are not prevalent. To solve this problem, we aimed to establish chromatographic condition to resolve MDA-TBA derivative for HPLC and LC-MS/MS analyses. First, most prevalent solvents such as 0.1% formic acid and 0.1% formic acid in acetonitrile were used to resolve MDA-TBA derivative by reversed phase HPLC. However, no peaks appeared by injection of MDA-TBA derivative. Similarly, red color substances remained in a solid extraction column (Sep-Pak C18) after elution with 0.1% formic acid and 100% acetonitrile but eluted with 75 mM ammonium acetate containing 50% acetonitrile. Based on these results, 200 mM ammonium acetate was added to water and 80% acetonitrile. For the first few times, the MDA-TBA derivatives and its byproducts were resolved by reversed-phase HPLC using this elution condition. However, after several injections, resolution of the MDA-TBA derivative became poor and finally it could not be eluted from the column. Injection of 1 M ammonium acetate into the column during washing with 200 mM ammonium acetate-80% acetonitrile generated large red peaks, indicating that MDA-TBA derivative and its byproducts remained in the column under this condition. Based on this result, the byproducts remained in the column were eluted with 200 mM ammonium acetate-80% acetonitrile and injection of 1 M ammonium acetate after elution of MDA-TBA derivative by the same solvents. This method enables reproducible resolution of MDA-TBA and can be used for HPLC and LC-MS/MS methods. This LC-MS/MS method provides sensitive and robust determination of MDA in biological samples at LOQ >10 nM. This method was applied to evaluate MDA levels in mouse after ingestion of glucose and fructose. After ingestion of fructose (2 g/kg), MDA levels in mice blood plasma and kidney increased approximately to 0.2 μM and 8 μmol/kg, respectively, and were significantly higher than those after ingestion of same dose of glucose, which reveals that fructose induces peroxidation of lipid compared to glucose.

A novel protein CYTB-187AA encoded by the mitochondrial gene CYTB modulates mammalian early development

Zhijuan Hu（胡志娟）

Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences,510530

**Correspondence email: hu_zhijuan@gibh.ac.cn*

Abstract

The mitochondrial genome has generally been understood to contain 37 genes, including 13 genes coding for proteins, 22 genes coding for transfer RNAs (tRNA) and 2 genes coding for ribosomal RNAs (12S and 16S rRNAs). The mitochondrial genome transcribes 13 mRNAs coding for well-known proteins essential for oxidative phosphorylation. In animal cells, there are two sets of "DNA-RNA-protein" central laws, which are encoded by two sets of genomes in the nucleus and mitochondria respectively. However, whether there is an intersection between the two sets of central laws: whether the mitochondrial genome can use the cytoplasmic ribosome to translate new proteins is one of the most basic scientific issues in life sciences. We demonstrate here that cytochrome b (CYTB), the only mitochondrial-DNA-encoded transcript among complex III, also encodes an unrecognized 187 amino-acid-long protein, CYTB-187AA, using the standard genetic code of cytosolic ribosomes rather than the mitochondrial genetic code. After validating the existence of this mtDNA-encoded protein arising from cytosolic translation (mPACT) using mass spectrometry and antibodies, we show that CYTB-187AA is mainly localized in the mitochondrial matrix and promotes the pluripotent state in primed-to-naïve transition by interacting with SLC25A3 to modulate ATP production. We further generated a transgenic knock-in mouse model of CYTB-187AA silencing and found that reduction of CYTB-187AA impairs females' fertility by decreasing the number of ovarian follicles. For the first time we uncovered a novel mPACT pattern of a mitochondrial mRNA and demonstrated the physiological function of this 14th protein encoded by mtDNA.

A novel redox gene *atad-3* identified by whole genome RNAi screen in *Caenorhabditis elegans*

Jiao Meng [1]（孟姣）,Xiaopeng Li[1] and Chang Chen[1]*

[1]Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Redox homeostasis is very important for normal cellular maintenance, and is closely related to cell growth, development, differentiation and senescence. Although some redox regulatory genes have been discovered, it is still far from clear how the redox network is accurately maintained and regulated in cells, and which genes are involved in regulation. Mitochondria are the most important source of ROS generated by electronic leak from the mitochondrial respiratory electron-transport chain, particularly mitochondrial Complexes I and III. Therefore, it is necessary to systematically screen new mitochondrial redox-related genes and investigate their functions. In this study we used an efficient Caenorhabditis elegans strain marked with the redox-sensitive probe mt-Grx1-roGFP2 located in body muscle mitochondria and executed a whole genome RNAi screening for mitochondrial redox related genes based on the COPAS biosort flow cytometer. We found that knock-down of atad-3 (ATPases associated with diverse cellular activities) generated more ROS via decreasing the proton leak and reducing mitochondria ETC complex I activity. Proteins interaction indicated that ATAD-3 had directly interaction with ETC complex I subunit NDUFS8 to affect the ETC complex I assembly and activity. ROS induced by atad-3 knockdown could activate the antioxidant system and enhance the stress tolerance of nematodes. In conclusion, this study combines redox probes with high-throughput screening. On the one hand, it provides a new strategy for genome-wide screening of redox regulatory genes, and a variety of different probes can be widely used for screening in the future. On the other hand, a new redox gene was discovered that play an important role in regulating redox signals by influencing the electron transport chain of mitochondria, which is of great significance in demonstrating the precise redox regulatory network.

Key Words: Redox-related gene, genome-wide screen, mitochondria

Elucidating the reducibility of sulfur dioxide on cysteine proteomes

Zongmin Li[1]（李宗敏）, Mengzhao Li,[2] Yaqian Huang,[1] Junbao Du,[1] Chunrong Liu,[2] Jing Yang,[3] Ling Fu,[3,] Hongfang Jin[1,4,*]*

[1]Department of Pediatrics, Peking University First Hospital, Beijing, 100034, China
[2]National Key Laboratory of Green Pesticide, College of Chemistry, Central China Normal University, Wuhan, 430079, China
[3]State Key Laboratory of Proteomics, Beijing Proteome Research Center, National Center for Protein Sciences, Beijing, Beijing Institute of Lifeomics, Beijing 102206, China
[4]State Key Laboratory of Vascular Homeostasis and Remodeling, Peking University, Beijing 100910, China

**Correspondence email: jinhongfang51@126.com; flsmt@163.com.*

Abstract

Sulfur dioxide (SO2) is an endogenous gasotransmitter in mammals. To date, it has been thought to engage in diverse biological processes and show potential for therapeutic aspects, which may be related to its oxidation-reduction property, but this is not yet clear. Here we propose that SO2 could exhibit reducibility towards proteinous cysteines by increasing the content of the reduced sulfhydryl groups (-SH) under physiological concentration, and verify this point from small molecule, recombinant protein models, to proteome level. Moreover, a site-specific chemoproteomic platform, called 'QTRP' (quantitative thiol reactivity profiling), is applied to establish the redoxome database and estimate the reducing capacity of SO2 on six cell lines, resulting in the quantification of overall 15,925 cysteines on 6,210 proteins, of these, the reduced sulfhydryl levels of nearly 22% of the sites were significantly increased by SO2. Gene ontology classification revealed that SO2-sensitive proteins are involved in numerous biological processes and pathways, including cell cycle, TCA cycle, autophagy, phosphorylation, and cellular response to oxidative stress. Based on this database, we uncovered a novel mechanism by which SO2 can alleviate oxidative stress in cardiomyocytes. Specifically, SO2 can act by disengaging the Kelch-like ECHassociated protein 1 (Keap1) dimer, subsequently facilitating the translocation of NF-E2-related factor 2 (Nrf2) into the nucleus. This leads to the upregulation of antioxidant protein expression, effectively rescuing the cells from oxidative stress. These findings reveal the chemical mechanism of SO2 action and expand the targeted cysteinous landscape, paving the way for understanding its biological functions comprehensively.

Exploring the collaboration of redox and autophagy systems based on a genome-wide new redox genes screening

Xinhua Qiao[1]（乔新华）, Miaomiao Guo[1], Mingxi Hu[1], Xiaopeng Li[1], Chang Chen[1,2]*

[1]Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China
[2]University of Chinese Academy of Sciences, Beijing 100049

**Correspondence email:changchen@moon.ibp.ac.cn*

Abstract

Background: The redox system is crucial for cellular homeostasis, and the discovery of new redox genes is a requirement for the field of redox. The development of redox probes and genome-wide screening technologies have enabled the execution of new genes screening.

Methods: Employing ratiometric redox probe Grx1-roGFP2 sensing GSH/GSSG, located in mitochondria of somatic muscles in *Caenorhabditis elegans*, we performed a genome-wide RNAi screening new regulators for glutathione redox status.

Results: We obtained 116 candidate GSH/GSSG regulated genes. Surprisingly, 28% of genes were involved in the autophagy pathway. Autophagy and redox both play crucial roles in stress response. However, whether and how the two systems collaborate remains unclear. Defects in a cluster of autophagy genes consistently led to increased GSH/GSSG levels. To further address the underlying mechanisms, we detect the genes mediating glutathione synthesis, degradation, transportation, and conjugation in four autophagy gene mutants, and found that the EGFR/EOR-1/GST-4 signaling pathway involved in the interplay between autophagy and redox systems. We further demonstrated that the elevation of GSH/GSSG levels served as a compensatory mechanism to enhance the survival and health of autophagy-deficient organisms under oxidative stress and in Alzheimer's disease model.

Conclusion and significance: In this study, we obtained new redox regulators based on a genome-wide screening, and highlighted the collaboration of autophagy and redox systems in maintaining cellular homeostasis via a unified signaling pathway. Our results provide valuable insights into the complex interplay between these systems and their role in cellular stress response, and may offer potential intervention prospects for diseases associated with autophagy defects and oxidative stress.

Key Words: Genome-wide screening, redox gene, autophagy, EGFR/EOR-1/GST-4

TRPC6-mediated Zn2+ influx improves heart failure through supersulfide formation

Xinya Mi[1], Chenlin Su[1], Tomoya Ito[1], Yuri Kato[1], Akiyuki Nishimura[2,3,4], Ryu Nagata[5], Yasuo Mori[6], Takaaki Akaike[7], Motohiro Nishida [1,2,3,4]

1) Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka 812-8582, Japan
2) National Institute for Physiological Science (NIPS), National Institutes of Natural Sciences (NINS), Okazaki 444-8787, Japan
3) Exploratory Research Center on Life and Living Systems (ExCELLS), NINS, Okazaki 444-8787, Japan
4) SOKENDAI (The Graduate University for Advanced Studies), Okazaki 444-8787, Japan
5) Graduate School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan
6) Graduate School of Engineering, Kyoto University, Kyoto 606-8501, Japan
7) Tohoku University Graduate School of Medicine, Sendai, Japan

**Correspondence email: mixinya@phar.kyushu-u.ac.jp*

Abstract

A growing body of evidence suggests that transient receptor potential canonical (TRPC) 3 and 6 channels are involved in developing pathological remodeling of the heart. However, we found that activation of TRPC6 channel enhances β adrenoceptor (βAR)-stimulated myocardial positive inotropy and prevents chronic heart failure in mice by enhancing Zn2+ dynamics. This study aims to investigate whether TRPC6-mediated Zn2+ influx suppresses sympathetic overactivity-induced chronic heart failure in mice. Chronic stimulation of βAR with intraperitoneal (i.p.) administration isoproterenol (ISO; 30 mg/kg/day) for 4 weeks caused myocardial dysfunction in WT mice and Zn2+ permeation-dead (PD) TRPC6 mutant-expressing mice. Treatment with 2-[4-(2,3-dimethylphenyl)-piperazin-1-yl]-N-(2-ethoxyphenyl) acetamide (PPZ2), a TRPC3/6/7 channel activator, improved ISO-induced heart failure in WT mice but failed in TRPC6 (PD) mice. Based on the comparison of amino acid sequences among TRPC3, TRPC7 and TRPC6 pore regions, we selected TRPC6-specific amino acid sequences and examined their relationship with Zn2+ permeability. We identified a Zn2+ permeation dead TRPC6 (PD) mutant using electrophysiological analysis. The TRPC6 (PD) mutant could permeate Na+, Ca2+ and K+ as much as wild type (WT) TRPC6 but failed to permeate Zn2+ after stimulation with PPZ2. Zinpyr-1 imaging revealed that PPZ2 increased the intracellular Zn2+ pool in ISO-treated WT hearts, while this increase was not observed in ISO-treated TRPC6 (PD) hearts. PPZ2 also improved ISO-induced impairment of L-type Ca2+ channel current and APD90 in WT mice but failed in TRPC6 (PD) mice. Furthermore, the live staining of heart tissue using SSip-1 DA (supersulfide) and SF7-AM (hydrogen sulfide) revealed that PPZ2 attenuated ISO-induced supersulfide intensity as well as the QS-10 (supersulfide) staining of neonatal rat cardiomyocytes suggesting PPZ2-induced Zn2+ influx through TRPC6 channel play a role in supersulfide catabolism. These results strongly suggest Zn2+ influx by pharmacological activation of TRPC6 channels improves heart failure associated with supersulfides.

TRPC6-mediated Zn^{2+} influx mitigates cardiac fibrosis through maintaining redox homeostasis

Chenlin Su[1], Xinya Mi[1], Tomoya Ito[1], Yuri Kato[1], Akiyuki Nishimura[2,3,4], Ryu Nagata[5], Yasuo Mori[6], Motohiro Nishida [1,2,3,4]

1) Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka 812-8582, Japan
2) National Institute for Physiological Science (NIPS), National Institutes of Natural Sciences (NINS), Okazaki 444-8787, Japan
3) Exploratory Research Center on Life and Living Systems (ExCELLS), NINS, Okazaki 444-8787, Japan
4) SOKENDAI (The Graduate University for Advanced Studies), Okazaki 444-8787, Japan
5) Graduate School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan
6) Graduate School of Engineering, Kyoto University, Kyoto 606-8501, Japan

**Correspondence email: su.chenlin.156@s.kyushu-u.ac.jp*

Abstract

Cardiac fibrosis mainly contributes to the development of chronic heart disease, and the progression of fibrosis reduces tissue compliance and worsens the severity of heart failure. A growing body of evidence suggests that Ca^{2+} influx through transient receptor potential canonical (TRPC) 3 and 6 channels participates in the progression of cardiac fibrosis. In contrast, TRPC6 channel has a unique characteristic in Zn^{2+} permeability, and we recently found that pharmacological activation of TRPC6 channel mitigates pressure overload-induced cardiac fibrosis and maintains Zn^{2+} pool in mouse hearts. This study aims to investigate whether TRPC6-mediated Zn^{2+} influx mitigates cardiac fibrosis in mice.

Wild type (WT), TRPC-deficient ($TRPC6^{(-/-)}$and $TRPC3^{(-/-)}$) mice were intraperitoneally implanted with osmotic pump including isoproterenol (ISO, 30 mg/kg/day for 4 weeks). Sirius red staining of heart sections and qPCR results showed that chronic ISO treatment significantly induced cardiac fibrosis in $TRPC6^{(-/-)}$ mice, compared with WT and $TRPC3^{(-/-)}$ hearts. Intraperitoneal treatment with 2-[4-(2,3-dimethylphenyl)-piperazin-1- yl]-N-(2-ethoxyphenyl) acetamide (PPZ2), a TRPC3/6/7 channel activator, improved ISO-induced cardiac fibrosis in WT mice, suggesting that TRPC6 channel activity negatively regulates cardiac fibrosis. Additionally, the electrophysiological study demonstrated that PPZ2 improved TGFβ-induced impairment of TRPC6 current in TRPC6-overexpressing cells. The α-SMA levels were detected with immunofluorescence and qPCR to explore anti-fibrotic effect of PPZ2 in adult cardiac fibroblasts (ACFs). PPZ2 prevented the TGFβ-induced fibrotic responses accompanied by the decrease of reactive oxygen species (ROS) production and increase of Zn^{2+} pool in ACFs isolated from WT mice but failed in $TRPC6^{(-/-)}$ mice. It is consistent with the in vivo results of ROS production determined by dihydroethidium staining and malondialdehyde level, that PPZ2 attenuated oxidative stress induced by chronic ISO treatment in heart. In conclusion, these results suggest that activating TRPC6-mediated Zn^{2+} influx improves cardiac fibrosis by maintaining redox homeostasis.

Detection of Protein Tyrosine Nitration or Amination

Jinwen Yang（杨劲文）*

Huazhong University of Science and Technology

**Correspondence email: yangjinwen0010@163.com*

Abstract

The generatipn of 3-nitrotyrosine (3-NT) on proteins is a common post-translational modification (PTM) that occurs in the state of redox homeostasis in the body. The increase of protein tyrosine nitration (PTN) level in tissues is closely related to the occurrence and development of many diseases we face. 3-amino-tyrosine (3-AT) was originally studied as a reduction product of 3-NT in vitro, but recent studies have shown that a certain enzymatic reduction process in vivo can also promote the transformation of nitro group to amino group, resulting in the production of protein tyrosine amination (PTA) modification process. Identifying PTN and PTA is the basis of understanding the pathologic mechanism related to PTN and revealing the effect of PTA on PTN signal transduction. Based on this, we developed a new two-step, one-pot strategy for the selective derivation of nitrotyrosine-containing and amino-tyrosine-containing proteins. First, 3-nitrotyrosine is reduced to 3-amino-tyrosine, and then 3-amino-tyrosine acts with 2-hydroxy-1-naphthalal and aluminum ions to form fluorescent complexes. The labeling strategy in this study has simple steps, low cost, strong specificity, mild reaction conditions, and no need to synthesize complex molecular probes. In the detection of protein samples, the polyacrylamide protein gel can be incubated directly with the mixed solution of 2-hydroxy-1-naphthalal and aluminum ion, and the 3-AT protein labeling at pmol level can be realized. This study provides a new detection method for the identification of PTN and PTA, which lays a solid foundation for further research on the correlation of these PTMS in cell function and pathology.

Key Words: Protein tyrosine nitration,Protein tyrosine amination

Discovery of small molecule inhibitors specifically targeting the Ero1α-PDI oxidative protein folding pathway

*Shuo Sun（孙硕）, Xi Wang, Chih-chen Wang, Lei Wang**

National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China

**Correspondence email: wanglei@ibp.ac.cn.*

Abstract

The endoplasmic reticulum (ER) oxidoreductin-1α (Ero1α) and protein disulfide isomerase (PDI) constitute the pivotal oxidative protein folding pathway in the ER, which is involved in various diseases including cancers, thrombosis and inflammation. Although several inhibitors targeting the individual Ero1α or PDI molecule were developed during the past decade, their specificity and effectiveness *in vivo* are still not verified. In this study, we first develop a high-throughput two-round *in vitro* screening system based on the Ero1α-PDI activity and identify two candidates (F7-6 and G7-10) from an FDA-approved drug library. F7-6 and G7-10 block the Ero1α-PDI complex formation, and inhibit their inter-molecular electron transfer *in vitro*. The two molecules don't inhibit the activity of other PDI family proteins such as ERp46, P5, and ERp57, showing high selectivity toward Ero1α-PDI system. We also show that F7-6 and G7-10 reversibly interfere with the Ero1α-PDI pathway *in vivo*, by employing a robust cell-based assay for detecting the ER redox homeostasis. Furthermore, they inhibit thrombin-stimulated platelet activation. Molecular docking and mutagenesis analysis reveal that the two small molecules bind to the hydrophobic pocket in *b'* domain of PDI, which is also the principal binding site for Ero1α. Altogether, F7-6 and G7-10 have been identified as novel Ero1α-PDI selective inhibitors, showing improved potency, favorable pharmaceutical properties, and therapeutic potential for antithrombotic therapy.

Key Words: Inhibitor, PDI, Ero1α, redox

Ferrocene Correlates with Ferroptosis: Multiple Approaches to Explore Ferrocene-appended GPX4 Inhibitors as Anticancer Agents

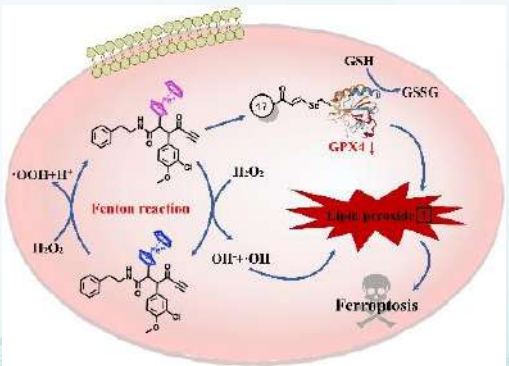
Yong WANG[a]（王勇）, Jing WANG, Wei Li, Xuejing FAN, Hui WANG, Jing LI*

Key Laboratory of Marine Drugs, Chinese Ministry of Education; School of Medicine and Pharmacy, Ocean University of China, Qingdao 26003, Shandong, P. R. China;

**Correspondence email: wangyong8866@ouc.edu.cn*

Abstract

Ferroptosis, which was defined in 2012 as an iron-dependent form of programmed cell death caused by increased cellular reactive oxygen species (ROS) and lipid peroxidation (LPO), exhibits remarkable promise for anticancer therapy.[1] We report a new series of ferrocenyl-appended GPX4 inhibitors as ferroptosis induces rationally designed in a "one stone kills two birds" strategy.[2] Ferroptosis selectivity assays, GPX4 inhibitory activity and CETSA experiments validated the inhibition of novel compounds on GPX4. In particular, the ROS-related bioactivity assays highlighted the ROS-inducing ability of **17** at the molecular level and their ferroptosis enhancement at the cellular level. These data confirmed the dual role of ferrocene as both the bioisostere motif maintaining the inhibition capacity of certain molecules with GPX4 and also as the ROS producer to enhance the vulnerability to ferroptosis of cancer cells, thereby attenuating tumor growth in vivo. This proof-of-concept study of ferrocenyl-appended ferroptosis inducers via rational design may not only advance the development of ferroptosis-based anticancer treatment, but also illuminate the multiple roles of the ferrocenyl component, thus opening the way to novel bioorganometallics for potential disease therapies.



Design, synthesis and antiparasitic activity of a novel naphthoquinone molecule based on SjTGR from Schistosoma Japonicum

Yongjie Zhang（张永杰）, Xiaolin Sun, Ning Lv, Chunyan Huang, and Xijing Chen

Clinical Pharmacology Research Center, School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University

**Correspondence email: zhangyongjie@cpu.edu.cn*

Abstract

S-glutathionylation (PSSG) is an essential type of protein post-translational modification, with the formation of disulfide bond between protein cysteine residue and glutathione. PSSG can occur chemically and enzymatically, in later cases glutathione S-transferase isoform P (GSTP) is the predominant enzyme facilitating the catalysis of PSSG. The substrate protein spectrum of PSSG is very board, including cytoskeletal proteins, enzymes and transporters, signaling proteins, transcription factors, chaperones, etc. In most cases, PSSG modification resulted the alteration of protein structures and functions to varying degrees, subsequentially influence physiological functions of cells and organs. PSSG reaction is mainly triggered by the elevation of oxidative potential, therefore the perturbation of PSSG is often observed in various oxidative stress-related diseases and drug toxicity reactions.

Over years, our group focused on the identification and characterization of PSSG process of key proteins in oxidative stress-related organ injury, *e.g.* acute lung injury (ALI) and oxidative stress-induced liver injury (OSILI), with the emphasis on the modulatory mechanisms of GSTP in the disease progression. Our results confirmed that Kelch-like ECH-associated protein 1(Keap1) and inhibitor of nuclear factor kappa-B kinase subunit β (IKKβ) were glutathionylated under ALI and OSILI status, and the functionally-essential glutathionylated cysteine sites in these two proteins were identified. Moreover, GSTP was shown to promote the PSSG process of Keap1 and IKKβ upon oxidative stimuli. It was suggested that GSTP-mediated PSSG process of Keap1 facilitated the downstream Nrf2 pathway activation and alleviated ALI and OSILI. On the contrary, PSSG of IKKβ under OSILI status was associated with a decreased resistance to the damage, suggesting a beneficial effect of GSTP inhibition in OSILI prevention and treatment. Collectively, this piece of work revealed novel regulatory mechanisms of GSTP and PSSG under ALI and OSILI conditions, which might be implicated in the discovery and development of therapeutic targets for oxidative organ injury.

Loss of poly(ADP-ribose) polymerase 1 boosts catalase activation via endothelin receptors

Jia-Bin Yu[1], *（于佳斌）* Daeun Moon[2], and Jinu Kim[1,2,*]

[1] *Interdisciplinary Graduate Program in Advanced Convergence Technology & Science, Jeju National University, Jeju, Jeju Self-Governing Province 63243, Republic of Korea*
[2] *Department of Anatomy, Jeju National University College of Medicine, Jeju, Jeju Self-Governing Province 63243, Republic of Korea*

**Correspondence email: jaibinyu46@gmail.com*

Abstract

Nephrotoxins have been identified as agents that can lead to acute kidney injury (AKI) with significant risks of morbidity and mortality. Poly(ADP-ribose) polymerase 1 (PARP1) plays a critical role in the cellular response to DNA repair, resulting in cellular ATP depletion and subsequently necrosis when excessively activated. This research seeks to explore the involvement of PARP1 in AKI induced by aristolochic acid through the use of *Parp1* gene-absent mice. The absence of *Parp1* significantly mitigated renal dysfunction and tubular injury caused by aristolochic acid exposure, as evidenced by reduced levels of plasma creatinine and blood urea nitrogen, as well as lower tubular injury scores spanning from the cortex to the inner medulla. Aristolochic acid triggered excessive poly ADP-ribosylation, with a small portion attributable to PARP1 activation in the kidneys, as indicated by a slight decrease in poly ADP-ribosylation in aristolochic acid-exposed *Parp1*-absent kidneys. *Parp1* absence resulted in hyperactivation of catalase and an upregulation of endothelin 1 in the kidneys. However, the inhibition of PARP1 activation did not affect catalase activation and ET1 expression in proximal tubular cells, suggesting that the absence of PARP1-dependent poly ADP-ribosylation is not linked to them. The administration of a catalase inhibitor substantially worsened aristolochic acid-induced kidney dysfunction and tubular injury in *Parp1*-absent mice. Additionally, blocking endothelin receptors eliminated the protective impact of *Parp1* absence against AKI, along with catalase hyperactivation. These results indicate that the absence of PARP1 offers protection against aristolochic acid-induced kidney injury via catalase hyperactivation induced by the upregulation of ET1.

Key Words: acute kidney injury; aristolochic acid; poly(ADP-ribose) polymerase 1; catalase

Myeloperoxidase (MPO) plays a key role in mitophagy in murine macrophages

Chaorui Guo（郭朝瑞）

China Pharmaceutical University

**Correspondence email: chaorui@cpu.edu.cn*

Abstract

Myeloperoxidase (MPO), a neutrophil-derived heme-containing peroxidase, plays an important role in the innate immune system. Numerous studies have proved that MPO and its main product, hypochlorous acid (HOCl), can cause extensive mitochondrial damage in various cell types, including macrophages, thus exacerbating diseases. Mitophagy is a critical process to maintain mitochondria homeostasis and protect against extensive cell damage. However, the role of MPO in mitophagy is still unclear and to be further clarified. We found LPS induced the conversion of LC3B-I to LC3B-II and co-localization of mitochondria with lysosomes in peritoneal macrophages in mice, which was not seen in Mpo-/- mice, showing that LPS-induced mitophagy may be MPO dependent. To investigate the underlying mechanism, murine macrophage cell line J774A.1 was treated with HOCl in vitro. Interestingly, HOCl could also induced conversion of LC3B-I to LC3B-II, and upregulated autophagy-related genes, LC3B, BECN and ATG5. Meanwhile, HOCl was shown to upregulate the expression of mitophagy-related genes, DRP1, PINK1, Parkin, OPA1, MFF and TFAM. Further in vivo and in vitro investigations showed that MPO and HOCl could stimulate phosphorylation of AMPK and ULK1. In J774A.1 cells, HOCl-induced phosphorylation of ULK1, and upregulation of DRP1, Parkin and PINK1 can be reversed by knockdown of AMPK using siRNA. Taken together, these results may indicate that MPO promoted mitophagy through AMPK/ULK1 pathway. In conclusion, this study suggests that MPO could induce mitophagy in murine macrophages, highlighting a novel role of MPO in innate immunity and diseases. These findings provide new insights into the mechanisms by which MPO contributes to cellular defense and pathology, potentially guiding future researches and therapeutic strategies.

Key Words: myeloperoxidase, mitochondria, autophagy, macrophage, AMPK pathway

$PM_{2.5}$ induced iron accumulation-associated liver injury via activation of ferroptosis and NLRP3 inflammasome

Lili Xin（信丽丽）, Weici Yan, Yue Su, Fei Jiang

Suzhou Medical College of Soochow University, 199 Renai Road, Suzhou 215123, Jiangsu, China

**Correspondence email: llxin@suda.edu.cn*

Abstract

Increasing evidence have pointed to a significant relationship between exposure to fine particulate matter ($PM_{2.5}$) and the incidence of liver damage and fibrosis. Ferroptosis, a newly recognized programmed cell death, was recently reported to be associated with liver diseases; recent studies demonstrated the contribution of NLRP3 inflammasome to the progression of liver diseases via inflammatory response as well. In this study, we investigated the possible role of ferroptosis and NLRP3 inflammasome in $PM_{2.5}$-induced liver damage using *in vitro* and *in vivo* models. Our results showed that $PM_{2.5}$ induced a notable dose-dependent cytotoxic effect on LO2 cells, mice liver injuries as well as increased levels of alanine aminotransferase and aspartate aminotransferase both *in vitro* and *in vivo*. These findings were accompanied by iron overload caused by the disruption of iron transport system and activation of NCOA4-mediated ferritinophagy. The excessive free iron subsequently induced ROS overproduction, GSH depletion, GPX activity loss, differential expression of Nrf2 signaling pathway elements, down-regulation of GPX4, lipid peroxides production and increasing expression of *PTGS2* and *ACSL4*, initiating ferroptosis cascades. In accordance with tissue inflammatory injuries, NLRP3/Caspase-1/IL-18/IL-1β pathway was activated by $PM_{2.5}$ exposure. The mitigating effects of deferoxamine on iron overload, redox imbalance, cell death, tissue injuries and NLRP3 inflammasome activation suggested ferroptosis and NLRP3 inflammasome as a potential molecular mechanism in $PM_{2.5}$-induced liver damage. Taken together, these results demonstrated that $PM_{2.5}$ induced liver cell death and tissue inflammatory injuries, which were mediated by activation of ferroptosis and NLRP3 inflammasome caused by iron-mediated oxidative stress. Our study provides new insights into the underlying mechanisms of $PM_{2.5}$-induced liver damage and predicts potential preventive strategies.

Polysulfides mediate multiple types of protein modification and tumor growth

Qingda Wang[1], Ting Lu[1,2], Luying Xun[2,3], Huaiwei Liu[2]（刘怀伟）*

[1]*Shandong University*

[2]*University of Health and Rehabilitation Sciences*

[3]*Washington State University*

**Correspondence email: liuhuaiwei@sdu.edu.cn*

Abstract

Polysulfides are sulfane sulfur (S^0) containing chemicals including hydrogen polysulfide (HS_nH, n≥2), glutathione polysulfide (GS_nH, n≥2), cysteine polysulfide (Cys-S_nH, n≥2), and octasulfur (S_8). In recent years, it has been found that polysulfides are widely present in all types of cells and involve in multiple physiological processes such as mitochondrial energy metabolism, embryonic development, cardiac function, and tumorigenesis, but the functioning mechanisms are largely unknown. In our study, we discovered that polysulfides can efficiently mediate protein disulfide bond formation, S-glutathionylation (Pr-SSG) formation, as well as protein polysulfidation formation (Pr-S_nH). These modifications can be formed via directly reacting with polysulfides without the presence of oxygen. We knocked out two polysulfides metabolizing enzymes, sulfide: quinone oxidoreductase (SQR) and thiosulfate sulfurtransferase (TST), individually in HCT116 cells and found that both SQR and TST knockout diminished mitochondrial function, impaired cell proliferation, and triggered early apoptosis. Moreover, their knockout led to markedly reduced tumor sizes in mice models of colon xenografts. Thus, our study indicates that polysulfides play a critical role in tumor growth and polsulfides metabolizing enzymes are potential targets for tumor treatment.

Targeting the integrated stress response and redox balance is a new strategy in meningioma inhibiting

Yuanyuan Wang[1] *（王圆圆）, Chang Chen*[1, 2*]

[1] *Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China;*[2] *University of Chinese Academy of Sciences, Beijing 100049, China*

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Meningiomas constitute the most frequent and challenging neoplasms of the central nervous system, characterized by high recurrence rates, considerable surgical risks, and a notable lack of effective pharmacotherapeutics. This clinical dilemma underscores the urgent need to elucidate novel mechanistic pathways and therapeutic interventions. In our comprehensive analysis of clinical tissue specimens from meningioma patients, we discerned a marked dysregulation characterized by heightened expression of components associated with the integrated stress response (ISR) and an activated redox state. Motivated by these findings, we synthesized a distinctive compound, D1, designed to target and modulate these newly identified therapeutic avenues. Our multifaceted investigations spanning cellular assays, organoid models, and in vivo experiments convincingly demonstrate that D1 precipitates apoptosis in meningioma cells through its dual mechanisms of ISR antagonism and the perturbation of redox homeostasis. Crucially, corroborative assays affirm that both the ISR and redox equilibrium are pivotal to the adaptive survival strategies employed by meningioma cells, revealing their integral roles in tumor proliferation. In conclusion, our findings unveil the potential of specifically targeting ISR and redox equilibrium as a novel therapeutic approach for meningioma suppression. The development of the promising compound D1 represents a significant advancement that could shed the light on drug discovery and treatment regimens for meningiomas.

Key Words: Meningioma, Integrated Stress Response, Redox Balance, Regimens

Short CV

Yuanyuan Wang, PhD, is a postdoctoral at the Institute of Biophysics, Chinese Academy of Sciences, specializing in the molecular mechanisms and application transformations in redox biology. Research published in *Redox Biology* (2022, 2023), *Science China Life Sciences* (2023), *Free Radical Biology and Medicine* (2021), and *Antioxidants & Redox Signaling* (2021). Received awards contain "Youth Report Award" at 2021 SFRR-China Conference and the "Excellent Report Award" at the 2022 Progress of Biochemistry and Biophysics Forum. She also presented orally at the 2023 National Conference of Redox Biology and Medicine.

Analysis of Aging Biomarkers and Construction of a Physiological Age Prediction Model Based on Cytokine Profiling

Lvtao Zeng[a]（曾律滔）, Guoqing Fan[a], Sijia Li[a], Zihui Wang[a], Xin Gao[a], Yamin Dang[a], Yaqing Ma[a], Ju Cui[a], Jianping Cai[a].

a The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Beijing Hospital, National Center of Gerontology, National Health Commission, Institute of Geriatric Medicine, Beijing, China, 100730.

**Correspondence email: zengtiancai@sina.com (Lvtao Zeng), caijp61@vip.sina.com (Jianping Cai).*

Abstract

Objective: This study aims to explore the differences in cytokine levels across various age groups during aging and their relationship with the aging process, and to construct and validate a cytokine-based aging clock model.

Methods: We first used a cytokine antibody array capable of detecting 1,000 cytokines to analyze plasma samples from 120 individuals in an aging cohort. Cytokines were selected using linear correlation analysis and Bootstrap-Lasso regression to build an initial cytokine aging clock model. Subsequently, a customized cytokine chip was employed to detect the selected cytokines in 1,325 individuals. Spearman correlation analysis and Logistic regression were used to examine the relationship between cytokines, laboratory test indicators, and self-reported diseases. Additionally, ELISA was used to validate aging biomarkers in mouse serum.

Results: We identified 18 cytokines in males and 10 cytokines in females. The aging clock models showed a correlation coefficient of 0.98 and a root mean square error (RMSE) of 3.64 for predicting age in males, and a correlation coefficient of 0.971 and RMSE of 4.45 for females. In a larger population validation, 13 cytokines in males and 6 cytokines in females showed consistent trends. Using these cytokines to rebuild the aging clock and applying it to the larger dataset, the models yielded a correlation coefficient of 0.68 and RMSE of 11.11 for males, and a correlation coefficient of 0.74 and RMSE of 10.89 for females. Significant correlations were also found between cytokines and laboratory test indicators. Logistic regression revealed that the acceleration of aging (Δ age) was associated with self-reported diseases.

Conclusion: This study identified 13 cytokines in males and 6 cytokines in females as potential aging biomarkers. An aging clock was established that can be used to assess disease risk in individuals.

Key Words: Cytokines, Antibody Array, Aging Biomarkers, Aging Clock, Machine Learning.

Physiologically relevant Fenton-like reactions and redox cycles of labile iron species: implications for ferroptosis and Alzheimer's disease

Zhongwei Zhao[1,2]（赵仲伟）, Binglin Zeng[1], Peifeng Zhang[1], Can Wang[1], Zheng Wang[1], Nao Xiao[1]*

[1] School of Pharmaceutical Sciences, Capital Medical University, Beijing, China;
[2] College of Life Science and Technology, Beijing University of Chemical Technology, Beijing, China

**Correspondence email: zzhao@ccmu.edu.cn*

Abstract

In human blood plasma and within the cells, there is a redox-active (labile) iron pool that consists of iron(II) complexes with physiological ligands,[1] including iron(II)-histidine,[2] iron(II)-citrate,[3] and iron(II)-phosphate complexes,[4] and we[1-3] and other researchers[4] have shown that these iron(II) complexes can participate in the Fenton-like reactions to generate the most deleterious reactive oxygen species (ROS), hydroxyl radical, resulting in oxidation of the iron(II) complexes to their iron(III) forms.[1-4] Subsequently, these iron(III) complexes can be reduced back to their iron(II) forms by ascorbic acid and glutathione under physiological condition, which catalyzes the redox cycles of the iron species and in turn provides continuous generation of hydroxyl radicals in the presence of sufficient endogenous H_2O_2.[1] Hydroxyl radical can instantaneously react with biomolecules and cause various oxidative damages to nucleic acids, proteins and cells.[1] In a lipid environment, hydroxyl radical attacks can cause lipid peroxidation, which can lead to ferroptosis, a form of cell death induced by iron-dependent lipid peroxidation. Interestingly, a recent study indicates that Fenton reaction may play important role in producing the trigger waves for ferroptotic cell death.[5] Ferroptosis is likely one of the drivers of neurological cell death in Alzheimer's disease (AD), and elevated level of redox-active iron has been suggested to trigger the amyloid-β (Aβ) aggregation and oxidative damage in the brain. Iron(III)–histidine complexes, in particular, are found in Aβ plagues and neurofibrillary tangles in AD, and increased H_2O_2 production is also observed in the Aβ plagues.[2] We therefore suggest that these iron(III)–histidine complexes might be produced from the Fenton-like reaction between iron(II)–histidine complex and H_2O_2, and this reaction may play a potential role in the pathological process of AD.[2]

Key Words: Labile iron pool, Fenton-like reaction, Hydroxyl radical, Redox cycle, Ferroptosis, Alzheimer's disease

$PM_{2.5}$-induced premature senescence in HUVECs through the SIRT1/ PGC-1α/SIRT3 pathway

Jing Wu[a,]（武婧）, Meidi Gong[a], Juan Hu[a], Manman Lin[a], Xuecong Xu[a]*

Department of Toxicology, School of Public Health, Medical College of Soochow University, Suzhou 215123, Jiangsu, China

**Correspondence email: wujing88@suda.edu.cn*

Abstract

Vascular endothelial cell senescence plays a pivotal role in the development of atherosclerosis. Recent studies have demonstrated that ambient fine particulate matter ($PM_{2.5}$) induces stress-induced premature senescence (SIPS) in vascular endothelial cells. However, the precise mechanisms underlying this process remain to be fully elucidated. Cellular senescence is closely associated with reactive oxygen species (ROS), and emerging research has established a strong connection between the SIRT1/PGC-1α/SIRT3 signaling pathway and the antioxidant system in vascular endothelial cells. In this study, we aimed to investigate the impact of $PM_{2.5}$ on vascular endothelial cell senescence and to elucidate the underlying mechanisms. Our findings revealed that $PM_{2.5}$ exposure led to an increase in senescence-associated β-galactosidase (SA-β-gal) activity and the expression of the cell cycle-blocking proteins P53/P21 and P16 in human umbilical vein endothelial cells (HUVECs). Flow

cytometry analysis demonstrated an elevated proportion of cells arrested in the G0/G1 phase after $PM_{2.5}$ exposure. $PM_{2.5}$-induced cellular senescence was attributed to the disruption of the cellular antioxidative defense system through the SIRT1/PGC-1α/SIRT3 signaling pathway. The expression of cellular senescence markers was reduced after targeted scavenging of mitochondrial ROS using MitoQ. Moreover, treatment with SRT1720, a SIRT1-specific activator, upregulated the SIRT1/PGC-1α/SIRT3 signaling pathway, restored the antioxidant system, and attenuated the expression of cellular senescence markers. Taken together, our results suggest that $PM_{2.5}$ downregulates the SIRT1/PGC-1α/SIRT3 signaling pathway, resulting in impaired antioxidant defenses in HUVECs. Conclusion, allows for the accumulation of ROS, leading to inhibition of endothelial cell cycle progression and the onset of stress-induced senescence in HUVECs.

Key Words: Antioxidant defense, HUVECs, PM(2.5), SIRT1/PGC-1α/SIRT3 pathway, Stress-induced premature senescence

The Beneficial Effects of Knockout of Astrocytic Ceruloplasmin on Learning and Memory Function in Aging Mice

Zhong-Da Li[1,2,3]（李忠达）, Haiyan Li[1,4], Shaomeng Kang[1], Yang Li[2,3], Peng Yu[1,], Yan-Zhong Chang[1,*]*

[1]Ministry of Education Key Laboratory of Molecular and Cellular Biology, The Key Laboratory of Animal Physiology, Biochemistry and Molecular Biology of Hebei Province, College of Life Sciences, Hebei Normal University, Shijiazhuang, 050024, China
[2]Laboratory of Inflammation and Vaccines, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen, 518055, China.
[3]Laboratory of Immunology and Nanomedicine & China-Italy Joint Laboratory of Pharmacobiotechnology for Medical Immunomodulation, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen, 518055, China.
[4]College of Basic Medicine, Chengde Medical University, Chengde, 067000, China.

**Correspondence email: yupeng0311@163.com; chang7676@163.com*

Abstract

Ceruloplasmin (CP), as a multi-copper ferroxidase, is mainly synthesized by liver and secreted into the blood. Generally, CP in blood cannot cross through blood-brain barrier (BBB) into the brain. Previous studies confirmed that astrocytes can synthesize CP via a glycosylphosphatidylinositol (GPI) anchor in the brain, which may play an important role in the regulation of brain iron homeostasis. Iron deposition in brain occurred in the aceruloplasminemia patients, especially at the age of 45 y to 55 y, the neurodegenerative symptoms perform more obviously. In mice, *Cp* gene knockout can accelerate the pathology of neurodegenerative diseases via up-regulating iron contents, such as Alzheimer's Disease (AD) and Parkinson's Disease (PD). However, other studies reported that in 3-month-old $Cp^{-/-}$ mice, the iron contents in cerebral cortex, hippocampus and striatum were decreased. It is not clear what role CP plays in maintaining of brain iron homeostasis.

To further study the role of CP in brain iron metabolism, we used the cre-loxP system-mediated astrocyte-specific knockout CP mice as experimental materials, and obtained astrocyte-specific knockout CP ($Cp^{Gfap}cKO$) mice by hybridization with *Gfap-cre* transgenic mice and $Cp^{flox/flox}$ mice. The results showed that iron contents decreased in the cerebral cortex and hippocampus in $Cp^{Gfap}cKO$ mice, caused from the inhibition of iron release from the FPN1 on the basal surface of BMVECs. For the aged mice, the iron accumulation was slowed down by $Cp^{Gfap}cKO$ with aging. Then we detected learning, memory and recognitive abilities of 18-month-old $Cp^{Gfap}cKO$ mice by using Morris Water Maze (MWM) and New Object Recognition (NOR). To our surprise, astrocyte CP conditional knockout can improve the learning, memory and recognitive abilities in aged mice. Age-dependent iron deposition-induced MAPK/Erk and MAPK/p38 pathways are attenuated, resulting in decreased apoptosis. In addition, the weakening of MAPK/JNK pathway and the enhancement of PI3K/Akt/GSK3 pathway reduce the phosphorylation level of MYC, increase the nuclear translocation of MYC, resulting in reduced cell senescence. As a final result, the learning and memory abilities were improved.

Key Words: Ceruloplasmin; Astrocytes; Senescence; Lerning and memory; Brain iron metabolism

The changes of genes and protein which affects mitochondrial fusion and fission in AD transgenic mice

Anna Seino, *Takuma Hara and Koji Fukui*

Molecular Cell Biology Laboratory,
Graduate School of System Engineering and Science,
Shibaura Institute of Technology, Saitama 337-8570, Japan

**Correspondence email: mf23074@shibaura-it.ac.jp*

Abstract

In recent years, peoples with dementia have increased in Japan as the population ages, and it is predicted that 1/3 elderly people will have dementia by 2060. Alzheimer's disease (AD) accounts for approximately 70% of dementia means the reduction of Quality of Life not only for patients but also for those around them, the early detection and development of treatment are urgently needed.

Mitochondrial (mit) dysfunction has been widely reported to be associated with the onset of neurodegenerative disorders such as AD, but the detailed mechanisms are still unclear. In our previous study, we revealed that the expression of mitochondrial-localized heat shock protein 60 changes before and after neurite degeneration with proteomic analysis by using liquid chromatography-mass spectrometry/mass spectrometry. Furthermore, electron microscopy revealed numerous morphological abnormalities of mitochondria in neurites treated with hydrogen peroxide. Mitochondria normally undergo repeated processes of fusion and fission to maintain their morphology and function (mit dynamics). Because neurite alterations are observed in the early stages of AD in the brain, we hypothesized that neuronal dysfunction in AD may be due to the imbalance of fusion and fission mediated by mitochondrial membrane oxidation by reactive oxygen species. We analyzed mit dynamics-related proteins and genes.

We used 4 and 12-month-old C57BL/6J mice as the control (Ctrl) group and age-matched heterozygous and homozygous 5xFAD mice as the AD group. All mice were both male and female mice. After dissecting the mouse brain and hippocampus, we used reverse transcription quantitative polymerase chain reaction and Western blotting to identify changes in gene and protein expression. Blood samples were also collected during dissection for serum testing.

We confirmed changes in mit dynamics related genes and proteins between some groups, and additionally observed differences based on sex.

The molecular mechanism study of oxidized microRNA regulating P21 and promoting aging

Yingmin Zhang[1]（张英敏）, Jiaqi Guo[1,3],Xin Gao[1,2], Lan Yang[1], Ruomei Qi[1], Jianping Cai[1,2]*

1. The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Beijing Hospital, National Center of Gerontology, National Health Commission, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, 100730, Beijing, China;2. Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, 100730, Beijing, China; 3.University of Chinese Academy of Sciences, Beijing, 100049, China.

**Correspondence email: caijp61@vip.sina.com*

Abstract

P21 is an important aging-related protein and increases with aging,microRNAs targeting P21 gene 3'UTR can inhibit the level of P21 protein. During the aging process, the level of reactive oxygen species(ROS) increases, and these microRNAs may be oxidized, that is, o8G oxidative modification occurs and they lose the ability to regulate the P21 protein level. The regulatory role of oxidized microRNA in aging has not been reported. Here we found that in fibroblasts the ability to regulate P21 protein levels would decrease after the mutation of seed region G into U(o8G oxidative modification mimics) of hsa-miR-526b-3p and miR-106b-5p targeting P21 gene 3'UTR. It is speculated that the oxidation of these two microRNAs may be an important mechanism leading to the upregulation of P21 protein level in aging. In human fibroblast cells RNA-seq was used to find the changes after transfecting with hsa-miR-526b-3p.Then we verified that hsa-miR-526b-3p and miR-106b-5p could inhibit cell senescence through aging-related signaling pathways,such as cell cycle,autophagy,SASP and redox. While the G was replaced by U, the effect would be diminished. Subsequently we examine the role of oxidized microRNA in C57 mice. We also verified that microRNA with o8G oxidative modification will lose the ability to regulate p21 level to delay aging. At the same time they can target new genes to promote aging both in vitro and in vivo. Taken together, we have discovered a new mechanism for regulating aging, which may shed new light on anti-aging and aging-related diseases.

Key Words: P21 protein; ROS; Aging; microRNA; o8G modification

Disruption of E-prostanoid 3 receptor on cardiomyocytes protects against heart ischemia reperfusion injury

Dong He[1]（何东）, Jiahui Ge[1], Jinwei Guo[1], Gang Yu[1], Yingbi Zhou[1,], Bin Liu[1,*]*

[1]Cardiovascular Research Center, Shantou University Medical College, 22 Xin-Ling Rd, Shantou, 515041 China.

**Correspondence email: 327053552@qq.com*

Abstract

Background: Myocardial ischemia-reperfusion injury (I/R) frequently occurs in coronary artery disease. Inflammation and calcium overload are crucial mechanisms of injury. The E-prostanoid 3 receptor (EP3) is an important regulator of inflammatory response and has an effect on intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$). We have recently demonstrated that deficiency of EP3 on myeloid inflammatory cells alleviates renal I/R injury. However, how EP3 on cardiomyocytes is involved in myocardial I/R injury has not been clearly elucidated.

Methods: Wild type (WT), global EP3 knockout (*Ep3*$^{-/-}$), floxed *Ep3* (*Ep3*$^{F/F}$) and inducible cardiomyocyte-specific *Ep3* deletion (*Ep3*$^{F/F}$;*Myh6*^{MerCreMer}) mice (all on C57BL/6N background) were subject to sham operation or 30 min of ischemia followed by 24 h of reperfusion. Adult mouse cardiomyocytes were freshly isolated for *in vitro* research.

Results: The *Ep3* mRNA level in hearts was markedly increased after I/R. Transient antagonism of EP3 ameliorated myocardial I/R injury, which was mainly manifested by reduced infarcted area, serum LDH, CK, and CK-MB levels, and increased EF% and FS% values, while *Ep3*$^{-/-}$ mice failed to show similar protective effects. Mechanically, the tamoxifen-induced short-term disruption of EP3 in *Ep3*$^{F/F}$;*Myh6*^{MerCreMer} mice ameliorated I/R injury and also curbed the release of inflammatory cytokines including TNF- a , IL-6 ,and IL-1b, as the EP3 itself elevated $[Ca^{2+}]_i$ through non-Gi/PLC signaling pathway in cardiomyocytes. Meanwhile, *Ep3*$^{F/F}$; *Myh6*^{MerCreMer} mice that underwent the surgery 8 weeks after the tamoxifen treatment exhibited decreased cardiac function. Moreover, inflammation and the release of HMGB1 were increased in acute myocardial ischemia patients with successful percutaneous coronary intervention.

Conclusion: Activation of EP3 on cardiomyocytes increases $[Ca^{2+}]_i$ and exacerbates cardiac dysfunction after I/R, and transient antagonism of EP3 may be a potential therapeutic strategy to protect against myocardial I/R injury.

Key Words: EP3, Myocardial I/R injury, Ca^{2+}, Inflammation

The molecular mechanism of lysosome function impairment and promotes fat accumulation by loss of G6PD

Shanzhuang Niu（牛善状）

Yunnan University, 650091, No.2 Cuihu North Rd, Kunming City，Yunnan Province

**Correspondence email: niushanzhuang@163.com*

Abstract

Excessive fat accumulation contributes to the onset and progression of various human diseases, such as obesity and fatty liver, posing serious threats to human health and life. Glucose 6-phosphate dehydrogenase (G6PD) is a key enzyme involved in the biosynthesis of NADPH via the pentose phosphate pathway. The loss of G6PD function can cause an intracellular redox imbalance, leading to red blood cell dysfunction. Studies have shown that the loss of function of the G6PD-encoding gene *gspd-1* in *Caenorhabditis elegans* results in redox imbalance, triggers an oxidative stress response, and causes abnormal embryonic development. Simultaneously, the loss of *gspd-1* function activates phospholipases and disrupts glycerophosphate metabolism. Our findings indicate that the loss of *gspd-1* function in *C. elegans* increases reactive oxygen species (ROS) levels, reduces thiol content in vivo, and promotes fat accumulation in the intestine. Transcriptome sequencing revealed that the loss of *gspd-1* function leads to the suppression of lysosome-related gene expression and lysosomal dysfunction in *C. elegans*. Fluorescence experiments of lysosomal marker genes *scav-3p::scav-3::gfp* and *laat-1p::laat-1::gfp* showed that *gspd-1* RNAi reduced the number of lysosomes in the gut of *C. elegans*. Meanwhile, chloroquine was used to inhibit lysosomal acidification and fat activity. *gspd-1* RNAi causes fat accumulation.Using both *C. elegans* and mammalian cell models, this study investigates the role of G6PD-regulated redox balance in fat mobilization, elucidates the molecular mechanisms underlying lysosomal dysfunction caused by G6PD-related redox imbalance, and identifies the signaling pathways involved in fat accumulation driven by this imbalance. The study provides a scientific foundation for the clinical use of G6PD activators to treat fat accumulation-related diseases and offers potential drug targets for the development of treatments for these conditions.

Endogenous hydrogen sulfide promotes the proliferation and metastasis of breast cancer through PGK1 S-sulfhydration

Chenghua Luo（罗成华）, Mengmeng Zhao, Yalu Wang, Jianming Hu

Department of Pathology, Medical College, Shihezi University

**Correspondence email: 15700979599@163.com*

Abstract

Breast cancer is the sixth leading cause of cancer death in women in China. Endogenous hydrogen sulfide (H_2S) is involved in the occurrence and development of breast cancer, while its underlying mechanism is not yet clear. This study focused on the molecular mechanism of endogenous H_2S promoting the proliferation and metastasis of breast cancer, four major findings were revealed: (1) Inhibition of Cystathionine-β-synthase (CBS) and Cystathionine-γ-lyase (CSE) increased the content of glucose in the supernatant of breast cancer cell, and decreased the production of intracellular lactic acid and ATP . (2) Phosphoglycerate kinase 1 (PGK1) was S-sulfhydrated at Cys108 and Cys316 by H_2S, its S-sulfhydration level in breast cancer tissue was significantly higher than that in paracancerous tissue. (3) Blocked the S-sulfhydration of PGK1 inhibited glycolysis and malignant biological behaviors of breast cancer cell. (4) CSE inhibitor reduced the S-sulfhydration of PGK1 and inhibited the growth and metastasis of xenograft tumors, while NaHS reversed the effect of CSE inhibitor. This study detected a new mechanism that H_2S promoted breast cancer by S-sulfhydration of PGK1, thereby provided new therapeutic strategies for this disease.

Key words: breast cancer; H_2S; PGK1; S-sulfhydration

High PRDX4 Expression Can Predict Worse Pathological Characteristics in Cutaneous Squamous Cell Carcinom

Jia Han,[1,2]（韩佳）, Yangxian Zhang, [1,2,4] Yao Liu, [1,2,5] Xin Guo,[1,2,3] and Sohsuke Yamada[1,2]

[1]Department of Pathology, Kanazawa Medical University Hospital, Ishikawa, Japan; Tel: 81-76-2862211; hanj227@kanazawa-med.ac.jp, yangxian91220@163.com, tianqi11211216@163.com, sohsuke@kanazawa-med.ac.jp;
[2]Department of Pathology and Laboratory Medicine, Kanazawa Medical University, Ishikawa, Japan;
[3]Research Center, Hebei Province Hospital of Chinese Medicine, Affiliated Hospital of Hebei University of Traditional Chinese Medicine, Shijiazhuang, China.
[4]Department of Geriatrics, China-Japan Friendship Hospital, Beijing, China.
[5]Department of Pathology, the Fourth Hospital of Hebei Medical University, Shijiazhuang, China

**Correspondence email: Kimeru_hj@163.com*

Abstract

In Japan, cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer，aging increases its incidence drastically. Peroxiredoxin (PRDX) 4 is known to be closely related to the development and prognosis of many cancers according to our published papers. Also, we have recently reported that PRDX4 can improve the skin wound healing especially in aged mouse, and inferred that PRDX4 would probably affect the development of cSCC. In this study, we collected 150 patients' clinical data and surgical specimens with cSCC, and analyzed them with expression levels of PRDX4. We have preliminarily found that the high immunohistochemical expression of PRDX4(6%) predicts significantly worse pathological characteristics in cSCC patients.

Hydrogen Peroxide Turn on Heat as Thermogenic agents and signals: Cellular Thermoregulation in Physiologies and Pathphysiologies

Xu Zhang（张旭）

Zhengzhou University

**Correspondence email: johnsir@zzu.edu.cn*

Abstract

Hydrogen peroxide (H_2O_2) belongs to the group of reactive oxygen species (ROS) which are short-lived highly reactive molecules generated from molecular oxygen. In physiology, H_2O_2 can be reduced to H_2O catalyzed by peroxiredoxins, glutathione peroxidases, or catalase， accompanied by the oxidation of reduced equivalents (such as NADH, $FADH_2$, NADPH, and GSH). Thus, in theory, H_2O_2 is the partially reduced oxygen, and it may be the intermediate product of oxygen reduction, The energy released from the H_2O_2 pathway of oxygen redox cannot be used for ATP synthesis, but rather for thermogenesis or heat. Therefore, increased H_2O_2 flux will increase oxygen exertion, energy depletion, and thermogenesis. Extensively documents indicate that mitochondrial MnSOD (Manganese superoxide dismutase) and extra-mitochondrial NOX (NADPH oxidases) -could regulate H_2O_2 flux for cellular thermoregulation. Manganese superoxide dismutase (MnSOD) is in a product-inhibited state at physiological temperatures, whereas, it is specially activated by cold. In mitochondria, specifically cold-activated MnSOD pulls superoxide dismutation forward, resulting in increased H_2O_2 flux and thermogenesis. Over-generated H_2O_2 from MnSOD activation may be a second messenger to activate uncoupling for more thermogenic respiration in acute cold stress. So, MnSOD-dependent H_2O_2 regulates adaptive thermogenesis in Physiologies. NOX is especially activated in infection, resulting in an observed oxidative burst and superoxide anion generation. NOX-dependant superoxide is converted to hydrogen peroxide by efficient CuZnSOD in and outside cells. Superfluous hydrogen peroxide from the NADPH oxidation likely initiates the synthesis of prostaglandin E2. PGE2 stimulates more reduced equivalents to increase ATP synthesis and thermogenesis in their target cells. So, extra-mitochondrial hydrogen peroxide may be a pyrogenic mediator inducing fever in infection. In these cases, hydrogen peroxide flux is regulated by MnSOD and NOX to facilitate thermogenesis as thermogenic agents and signals.

Key Words: Hydrogen peroxide; Manganese superoxide dismutase; NADPH oxidases; Reactive oxygen species; Second messengers; Signaling. Prostaglandin E2

Increased oxidative stress induced by high-fat and high-fructose diets contribute to type 2 diabetes and its associated complications

Qing-Yu Wang[1,2]*（王清宇）, Yun-Wen Zhang*[1]*, Feng-Wang Xu*[1]*, Lan Yang*[1]*, Hui-Lian Chen*[1]*, Jian-Ping Cai*[1]

[1] *The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital/National Center of Gerontology of National Health Commission, Beijing, China, 100730.*
[2] *Medical Research Center, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China, 100020.*

**Correspondence email: daisyqingyu@outlook.com; caijp61@vip.sina.com*

Abstract

We established a rat model of type 2 diabetes mellitus (T2DM) using a long-term high-fat, high-fructose diet. We observed significant increases in reactive oxygen species (ROS) levels and oxidative damage to nucleic acids in systemic circulation and colonic epithelial tissues. Additionally, we detected abnormal proliferation of colonic stem/progenitor cells and an elevated number of colonic enteroendocrine cells (EECs). Focusing on EECs and given the observed impairment in GLP-1 production in elderly T2DM rats and humans, we employed single-cell transcriptome sequencing to investigate further. Our results revealed that the differentiation of EECs into GLP-1$^+$ EECs (L cells) is impaired in elderly T2DM rats, corresponding with the observed decreased GLP-1 production. This finding suggests new insights for the development of drugs aimed at increasing endogenous GLP-1 secretion, particularly for elderly T2DM patients who are prone to have impaired incretin effects. Regarding the findings related to stem/progenitor cells, we conducted oxidative miRNA sequencing and in vitro and in vivo experiments; we identified and validated that oxidative modification of miR-30c-5p leads to abnormal regulation of YB-1, which may be a crucial molecular mechanism underlying the increased risk of colon cancer in T2DM patients. These insights offer new perspectives for preventing and treating colon cancer in T2DM patients.

LPO-dependent lipid rafts inhibit immunogenic ferroptosis and pyroptosis in melanoma

Xi Zhao[1], Zenglu Zhao[1], Shuyu Huan[1], Zixi Li[1], Guoquan Liu[1,2]（刘国全）*

[1] State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing, China
[2] Institute of Advanced Clinical Medicine, Peking University, Beijing 100191, China

**Correspondence email: guoquanliu@bjmu.edu.cn*

Abstract

Chemotherapy including platinum-based drugs are a possible strategy to enhance the immune response in advanced melanoma patients who are resistant to immune checkpoint blockade (ICB) therapy. However, the immune-boosting effects of these drugs are a subject of controversy, and their impact on the tumor microenvironment are poorly understood. In this study, we discovered that lipid peroxidation (LPO) promotes the formation of lipid rafts in the membrane, which mediated by ACSL4 impairs the sensitivity of melanoma cells to platinum-based drugs. This reduction primarily occurs through the inhibition of immunogenic ferroptosis and pyroptosis by reducing cell membrane pore formation. By disrupting LPO-dependent lipid rafts via the removal of membrane cholesterol, we promoted immunogenic cell death, transformed the immunosuppressive environment, and improved the antitumor effectiveness of platinum-based drugs and immune response. This disruption also helped reverse the decrease in CD8+ T cells while maintaining their ability to secrete cytokines. Our results reveal that LPO is a key regulator of lipid rafts formation and antitumor immunity, and that disrupting lipid rafts has the potential to enhance platinum-based drug-induced immunogenic ferroptosis and pyroptosis in melanoma. This novel strategy may augment the antitumor immunity of platinum-based therapy and further complement ICB therapy.

Key Words: Ferroptosis; Pyroptosis; Lipid raft; Lipid peroxidation

Pharmacological targeting of NRF2 represents a promising therapeutic approach for ferroptosis-related diseases

Pengfei Liu, （刘朋飞） *Mengjiao Shi, Xinyan Li, Jiayi Xu, Yinggang Zhang.*

National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University

**Correspondence email: liupengfei@xjtu.edu.cn*

Abstract

Transcription factor nuclear factor-erythroid 2-like 2 (NRF2) is a key regulator of the cellular antioxidant response, redox homeostasis and metabolic balance. Ferroptosis is a novel type of cell death, which is different from apoptosis, necrosis or autophagic cell death. In recent years, lots of research has demonstrated that ferroptosis results from iron-dependent lipid peroxidation. The close connection between NRF2 and ferroptosis have been confirmed by several groups, and lots of genes which inhibits lipid peroxidation, the initiation of ferroptosis, have been identified as NRF2 target genes, such as HMOX1, GPX4 and SLC7A11. Besides, both glutathione synthesis and iron metabolism can also be regulated by NRF2 signaling pathway effectively. Therefore, the inhibition of NRF2 may be also necessary to enhance the sensitivity of cancer cells to ferroptosis. Mitochondria holds a key position in the regulation of cell signaling transduction and cellular metabolism. The most important role of mitochondria is to create energy via oxidative phosphorylation (OXPHOS). Some studies indicated that mitochondria play an important role in the ferroptosis induced by cysteine deprivation, but not in the ferroptosis induced by GPX4 inhibition. Besides, both tricarboxylic acid (TCA) cycle and mitochondrial electron transport chain (ETC) activity are necessary for the generation of lipid ROS in the ferroptosis induced by cysteine deprivation. Therefore, close association exists among NRF2, Mitochondria and Ferroptosis.

Our studies indicated that NRF2 suppression, and ferroptosis promotion are important molecular mechanisms in metabolic diseases and cancer. For example, NRF2 acts as a key player in the development and progression of fatty liver disease, and decreased autophagosome biogenesis, reduced NRF2, and enhanced ferroptotic cell death are underlying molecular mechanisms of non-alcoholic fatty liver disease. Pharmacological NRF2 activation counteracts high fat diet-mediated ferroptotic cell death in liver. In addition, the translational significance of NRF2-mediated transcriptional repression is illustrated in our previous work. We confirmed the negative regulation relationship between NRF2 and FOCAD, which was dependent on NRF2-RPA1-ARE complex. FOCAD promotes the activity of FAK, which further enhances the sensitivity of human non-small-cell lung carcinoma (NSCLC) cells to cysteine deprivation-induced ferroptosis via promoting the tricarboxylic acid (TCA) cycle and the activity of Complex I in mitochondrial electron transport chain (ETC). Moreover, the treatment with the combination of NRF2 inhibitor (brusatol) and erastin shows better therapeutic action against NSCLC in vitro and in vivo than single treatment, indicating that the combination of ferroptosis inducer and brusatol may be a promising therapy mode against cancer in clinic. Moreover, FOCAD-FAK signaling was further evaluated in the tumor tissues. We also found that brusatol treatment increased the level of FOCAD and promoted pAKT signaling via affecting NRF2, which was abolished by FOCAD knockout. Besides, the combination of brusatol and RSL3 didn't show different effect on ferroptosis in FOCAD-WT group and FOCAD-KO group, but the ferroptosis induced by signal erastin or brusatol+erastin was limited in FOCAD-KO group compared with FOCAD-WT group, indicating the key position of FOCAD in cysteine deprivation-induced ferroptosis. Meanwhile, the pre-treatment with either ferroptosis inhibitor (Fer-1) or mitochondria protective agent (DMF, NRF2 activator) relives isoflurane-induced ferroptosis as well as learning and memory impairment, indicating the significance of NRF2-dependent protection against ferroptotic cell death in neurological diseases. Totally, the crosstalk between NRF2 signaling and mitochondria is important in ferroptosis-related diseases, providing novel therapeutic strategy against metabolic diseases and cancer.

Key Words: NRF2, mitochondria, ferroptosis, metabolism, antioxidants.

Radix Rehmanniae and its Active Ingredients Ameliorate CFA-Induced Inflammation by Attenuating Macrophage-Mediated Localized Response and Nitrative Damage

Jie Chen[1,2†]（陈杰）,Lu Zhang[2†], Chengyu Zhuang[1]*, Jiangang Shen[1,3]*

1 Department of Orthopedics, Shanghai Institute of Traumatology and Orthopedics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, of China

2 School of Chinese Medicine, LKS Faculty of Medicine, the University of Hong Kong. Hong Kong, China

3 Shenzhen Institute of Research and Innovation, The University of Hong Kong, Shenzhen, China

**Correspondence email: shenjg@hku.hk*

Abstract

Osteoarthritis(OA)-related Inflammatory pain is a prevalent symptom in degenerative diseases affecting mature individuals, often presenting as persistent joint pain and impaired daily functioning. This pain is closely linked to tissue damage and immune cell infiltration. Targeting macrophage polarization, a process influenced by the local microenvironment emerges as a promising strategy for managing inflammatory pain.

Radix Rehmanniae (RR), also known as Sheng Di Huang in Chinese, is a traditional Chinese medicinal herb that has been utilized for centuries to treat various ailments, including inflammation-related conditions. In recent years, scientific research has been dedicated to comprehending the mechanisms and therapeutic potential of RR and its active compounds in the context of inflammatory pain and OA. However, its immuno-modulatory effects and anti-inflammatory properties in the context of inflammatory pain still need to be explored.

This study examined the in vivo and in vitro anti-inflammatory and antioxidant effects of RR and its active ingredients, as well as the role of macrophage polarization in attenuating OA-related inflammatory pain. Using the CFA-induced pain model, which effectively induces localized inflammation and pain, mirroring the symptomatic profile observed in conditions like OA. The results revealed that RR and its active ingredients had the significant analgesic effect, RR has exhibited the capacity to substantially reduce pain-associated behaviors, including heightened sensitivity to mechanical and thermal stimuli. These effects collectively enhance the overall quality of life for individuals grappling with inflammatory pain.

The production of reactive nitrogen and oxygen species, such as peroxynitrite, can result in oxidative and nitrative stress, which can cause damage to the cellular components. Our research delved into the effects of RR and its active compounds, intending to reduce nitrative damage and oxidative stress. This could aid in safeguarding the tissues from further harm and foster the resolution of inflammation.

Contributions to inflammatory pain and tissue damage are the activation and polarization of macrophages, the pivotal immune cells that regulate inflammation. Macrophages exhibit different activation states, with the M1-like phenotype linked to pro-inflammatory responses and the M2-like phenotype associated with anti-inflammatory processes and tissue repair. RR and its active compounds have demonstrated the ability to modulate macrophage polarization, favoring a transition from the M1-like to the M2-like phenotype. Further *in vitro* evaluations of RR and active ingredient effects on macrophage polarization were conducted using optimized culture systems. The result suggests that RR's inhibitory effects on macrophage-derived nitrative damage are linked to suppressing the TLR4-MyD88- nuclear factor kappa-light chain enhancer of activated B cells (NF-κB) pathway. Macrophage polarization and antioxidant effects were explored concerning mir155-mediated mechanisms.

In summary, this research highlights that macrophage-induced inflammation leads to localized nitration and assembly, contributing to tissue damage and inflammatory cell infiltration in OA pathogenesis. Targeting macrophage-mediated inflammation offers a promising OA therapeutic strategy. RR and its active ingredients show potential as therapeutic agents to alleviate macrophage-mediated localized inflammatory microenvironments and nitrative damage in OA treatment. Further investigations are warranted to comprehend the precise mechanisms and clinical applicability of RR and its active compounds in managing inflammatory pain and OA.

Key Words: Radix Rehmanniae, Osteoarthritis, Macrophage polarization, Inflammatory pain, Nitrative Damage

Redox regulated Mitophagy in Arsenite-induced Malignant Transformation of Human Keratinocytes

Qianlei Yang（杨乾磊）, Yan An

Department of Toxicology, School of Public Health, Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, MOE Key Laboratory of Geriatric Diseases and Immunology, Suzhou Medical College of Soochow University, Suzhou, Jiangsu 215123, P.R. China.

**Correspondence email: dranyan@126.com*

Abstract

Our previous research found that the reductive stress induced by nuclear factor erythroid-2 related factor 2 (NRF2) through glucose metabolic reprogramming promotes malignant transformation in Arsenite-exposed human keratinocytes (HaCaT). Autophagy-deficient cancer cells can survive through mitophagy, however, the molecular mechanisms underlying redox regulated mitophagy in arsenic-induced malignant transformation of HaCaT cells remains unclear. Herein, the dynamic changes of redox and PTEN induced putative kinase 1 (PINK1)-dependent mitophagy regulated by NRF2 during the malignant transformation were measured. It is found that $NaAsO_2$ exposure induced the imbalance of redox can continuously activate mitophagy. In detail, when the mitophagy inhibitor of cyclosporin A (CsA) is applied, or via *NRF2* siRNA transfection, the expressions of PINK1 and Parkin, as well as the number of mitolysosomes are significantly decreased, indicating that both CsA and *NRF2* silencing can inhibit mitophagy. While under the existence of mitophagy activator of carbonyl cyanide 3-chlorophenylhydrazone (CCCP), the above-mentioned indexes are reversely changed as expected, leading to the increased cell migration rate, soft agar clones, and shortened cell doubling time. Collectively, it is suggested that long-term exposure to arsenite promotes the malignant transformation of HaCaT cells via NRF2 activated PINK1/Parkin pathway-mediated dynamic mitophagy, which may provide a new research perspective for the exploration of possible molecular mechanism underlying arsenic-induced malignancy progression.

Role of miR-3689a-3p in the regulation of mitochondrial oxidative stress in the sorafenib resistance of hepatocellular carcinoma

Yau-Tuen Chan[1] , *Yuanjun Lu*[1] , *Ning Wang*[1]

[1] *School of Chinese Medicine, The University of Hong Kong*

**Correspondence email: eugene.chan@hku.hk*

Abstract

The effectiveness of sorafenib in treating hepatocellular carcinoma (HCC) is compromised by the evolution of drug resistance. The purpose of this study was to pinpoint the crucial microRNA (miRNA) that is accountable for sorafenib resistance at the genomic level. Our study investigated the role of miRNA miR-3689a-3p in mediating sorafenib resistance in HCC and how it interacts with tumor-suppressive, sorafenib induced mitochondrial reactive oxygen species (mtROS) production. Using CRISPR/Cas9 screening, it was found that miR-3689a-3p was up-regulated in sorafenib-sensitive HCC. Knocking it down increased resistance to sorafenib, while overexpression sensitized HCC to the treatment. By proteomics analysis, it was discovered that sorafenib-induced mtROS production, which tends to be tumor-suppressive, causes mitochondrial dysfunction. This could be regulated by disrupting the internal antioxidative system, mitochondrial copper-zinc superoxide dismutase 1 (SOD1), via miR-3689a-3p. This microRNA targets the SOD1, disrupting intracellular copper trafficking and reducing SOD1 activity, leading to HCC cell death in response to sorafenib. This indicates that miR- 3689a-3p is a critical factor for the sorafenib response in HCC cells and maintaining its level may enhance patient response to sorafenib treatment. Clinical implications suggest miR-3689a-3p as a potential target for improving sorafenib treatment in HCC.

Key Words: In vivo CRISPR/Cas9 screen, Sorafenib, MiR-3689a-3p, Drug resistance of hepatocellular carcinoma, CCS

S-nitrosylation enhances RhoA activity and promotes tumor cell invasion and metastasis

Zhouzhou Ye[1,2#], Chengbin Fu[3#], Yinyin Yao[1,2], Anhai Fu[1,2], Mingwei Cai[1,2], Huanzhang Xie[1,2], Chunlian Zhong[1,2*], Lee Jia[1,2*], Yusheng Lu[1,2*]（卢余盛）*

[1] *Fujian-Taiwan-Hongkong-Macao Science and Technology Cooperation Base of Intelligent Pharmaceutics, College of Material and Chemical Engineering, Minjiang University, Fuzhou, Fujian 350108, China*
[2] *Fuzhou Institute of Oceanography, Minjiang University, Fuzhou, Fujian 350108, China*
[3] *Department of Breast Surgery, Fujian Medical University Union Hospital, Fujian Medical University, Fuzhou 350001, China*

**Correspondence email: gxdym01@163.com (HZX); zhongchunlian0117@126.com (CLZ); cmapcjia1234@163.com (LJ); lu_yu_sheng@126.com (YSL)*

Abstract

RhoA, a member of the Ras homolog gene family, plays a critical role in regulating tumor cell invasion and metastasis by influencing cell morphology, adhesion to the extracellular matrix, and cytoskeleton organization. In our recent proteomic studies, we identified that the Cys20 residue of the RhoA protein undergoes S-nitrosylation, but the impact of this modification on RhoA's function and activity has not been previously explored. In this study, we investigated the effects of Cys20 S-nitrosylation on RhoA activity in tumor cells using cell lines engineered to overexpress either wild-type RhoA or mutant-type RhoA (Cys20 was replaced by Ser20). Our real-time cell analysis (RTCA) experiments demonstrated that S-nitrosylation enhances the invasive properties of tumor cells. Additionally, qRTPCR and western blot analyses revealed that S-nitrosylation, induced by GSNO, promotes the expression of epithelial-mesenchymal transition (EMT)-related proteins. RhoA-GTP enrichment assays further showed that S-nitrosylation significantly increases the formation of the active RhoA-GTP complex, indicating heightened RhoA activity. This was supported by computer simulations and molecular dynamics experiments, which confirmed that S-nitrosylation of Cys20, located in the GTP-binding pocket, strengthens the interaction between RhoA and GTP. In summary, our findings suggest that nitric oxide promotes the activation of RhoA by inducing S-nitrosylation at Cys20, leading to EMT and increased invasive and metastatic potential in tumor cells.

Key Words: RhoA; S-nitrosylation; Epithelial-mesenchymal transition (EMT); Cancer metastasis; Nitric oxide

The circ_0071616-miR-140-3p-USP34 axis mediates FoxM1 deubiquitination in Helicobacter pylori-induced gastric malignant transformation

Li Xize[1]*（李析泽）*, Wang Haocheng*[2], Zeng Jiping*[1*]

[1.]Department of Biochemistry and Molecular Biology, School of Life Sciences and Health, University of Health and Rehabilitation Sciences, Qingdao 266113;
[2.] Shanghai Jiao Tong University School of Medicine, Shanghai 200025; P.R.China.

**Correspondence email: zengjiping@uor.edu.cn*

Abstract

Helicobacter pylori infection can induce malignant transformation of gastric mucosal epithelial cells, and the role of "epigenetic reprogramming" involving environmental factors, abnormal expression heterogeneity of host genes, and regulation of tumor microenvironment in this process deserves attention. Both high-throughput sequencing and bioinformatics analysis results suggested that the pathway involved key nodes circ_0071616 / miR-140-3p / USP34 could affect cell proliferation and ubiquitin-related signal transduction in *helicobacter pylori* infection-related gastric malignant transformation. The results from qRT-PCR, Western blotting, EdU assay, CCK-8 assay, colony formation assay, SA-β-gal staining, and subcutaneous tumor formation experiment in nude mice demonstrated that circ_0071616 could promote gastric carcinogenesis by enhancing cell proliferation and inhibiting cell senescence. Online database prediction results along with luciferase activity detection, FISH experiment findings and correlation analysis of genes expression confirmed the direct binding between circ_0071616 and miR-140-3p as well as their functional interaction. TCGA database screening combined with cellular molecular experiments and animal model studies further validated miR-140-3p as a tumor suppressor in gastric cancer by inhibiting cell proliferation while promoting cell senescence. Subsequent investigations revealed that circ_0071616 regulated miR-140-p to directly bind to the core sequence within USP34 3'-UTR region leading to inhibition of the oncogenic molecule deubiquitinating enzyme USP34 expression thereby stabilizing FoxM1 protein levels which ultimately contributes to the gastric carcinogenesis and development. This study provides preliminary evidence for the mechanism of *Helicobacter pylori* infection on the deubiquitination process of FoxM1, a crucial positive regulatory protein in cell cycle regulation, through the circ_0071616 - miR-140-3p - USP34 pathway. These findings can offer novel insights into the early diagnosis and treatment strategies for gastric cancer.

Key Words: Cell Senescence; Epigenetic Reprogramming; Non-coding RNAs; Deubiquitination; *Helicobacter pylori*; Gastric Carcinogenesis

A Bayesian benchmark concentration analysis for urinary fluoride and intelligence in adults in Guizhou, China

Tingxu Jin（金庭旭），Yan An.

Suzhou Medical College of Soochow University.

**Correspondence email: lanting8310@sina.com*

Abstract

Environmental fluoride exposure has been linked to numerous cases of fluorosis worldwide. Previous studies have indicated that long-term exposure to fluoride can result in intellectual damage among children. However, a comprehensive health risk assessment of fluorosis-induced intellectual damage is still pending. In this research, we utilized the Bayesian Benchmark Dose Analysis System (BBMD) to investigate the dose-response relationship between urinary fluoride (U-F) concentration and Raven scores in adults from Nayong, Guizhou, China. Our re search findings indecate a dose-response relationship between the concentration of U-F and intelligence scores in adults. As the benchmark response (BMR) increased, both the benchmark concentration (BMCs) and the lower bound of the credible interval (BMCLs) increased. Specifically, BMCs for the association between U-F and IQ score were determined to be 0.18 mg/L (BMCL1 = 0.08 mg/L), 0.91 mg/L (BMCL5 = 0.40 mg/L), 1.83 mg/L (BMCL10 = 0.83 mg/L) when using BMRs of 1 %, 5 %, and 10 %. These results indicate that U-F can serve as an effective biomarker for monitoring the loss of IQ in population. We propose three interim targets for public pol icy in preventing interllectual harm from fluoride exposure.

Circadian-Cognitive Synchrony Disrupted: Iron's Influence on Rhythmic and Memory-Related Neural Functions

Qiong Wu[1,2]（吴琼） *Qiu-Yang Ren*[1] *Rui-Kun Xie*[1] *Xin Wang*[1] *Yan-Zhong Chang*[1#]

[1.] *Laboratory of Molecular Iron Metabolism, Key Laboratory of Molecular and Cellular Biology of Ministry of Education, Hebei Key Laboratory of Animal Physiology, Biochemistry and Molecular Biology, Hebei Collaborative Innovation Center for Eco-Environment, Hebei Research Center of the Basic Discipline of Cell Biology, College of Life Sciences, Hebei Normal University, Shijiazhuang, 050024, China.*

[2.] *Hebei Key Laboratory of Chinese Medicine Research on Cardio-Cerebrovascular Disease, College of Basic Medicine, Hebei University of Chinese Medicine, Shijiazhuang, 050200, Hebei Province, China.*

**Correspondence email: chang7676@163.com*

Abstract

Iron is crucial for numerous physiological processes, and its dysregulation can precipitate serious conditions such as neurodevelopmental impairments, neurodegenerative diseases, stroke, and cancer. The interplay between biological rhythms or contextual fear conditioning (CFC) and brain iron homeostasis remains understudied, leaving a gap in our understanding of iron's role in circadian-cognitive functions, particularly in CFC. This study aimed to investigate how varying brain iron levels impact the regulation of circadian rhythms and CFC, and to uncover the underlying mechanisms. Our findings demonstrate that cellular iron level alterations can modulate the circadian rhythm by affecting the expression of the period circadian regulator 1 (PER1), a key transcriptional repressor for biological rhythm regulation. In the realm of CFC, we discovered that increased Ferroportin 1 (FPN1) expression in brain microvascular endothelial cells at the blood-brain barrier facilitates iron entry into the brain, which in turn, during the formation of CFC in mice, elevates brain iron levels. This iron influx further promotes Lipocalin 2 (LCN2) expression, which in turn activates the conversion of brain-derived neurotrophic factor (BDNF) precursors to mature BDNF by matrix metalloproteinase-9 (MMP9). The enhanced BDNF then binds to tropomyosin receptor kinase B (TrkB), activating downstream synaptic plasticity-related proteins and bolstering the formation of contextual-fear memory. In summary, our research not only pinpoints the modulation of brain iron levels as a promising therapeutic target for age-related circadian rhythm disruptions but also sheds light on the intricate molecular underpinnings of CFC formation. This work offers novel perspectives for the clinical management of fear-related psychiatric disorders.

Mechanism analysis of oxidative stress and inflammation in brain diseases

Qianjin Liu（刘前进）

Xuzhou Medical University

**Correspondence email: liuqianjin@xzhmu.edu.cn*

Abstract

Oxidative stress and inflammation are associated with the development of several diseases, especially the brain diseases. We have done a systematic study on the role of oxidative stress and inflammation in brain diseases and found that oxidative stress and inflammation play important roles in Parkinson's disease (Natl Sci Rev 2021, Free Radical BioMed 2022), neurotropic virus infection (Redox Biol 2021) and morphine analgesia (Redox Biol 2020, Redox Biol 2024). We focus on protein nitrosylation induced by nitric oxide in oxidative stress. Recently, we demonstrated that S-nitrosoglutathione reductase (GSNOR) deficiency in macrophages leads to significant increases in the Nlrp3 and Il-1β expression levels and interleukin-1β (IL-1β) secretion in response to NLRP3 inflammasome stimulation. Furthermore, in vivo experiments utilizing Gsnor-/- mice revealed increased disease severity in both lipopolysaccharide (LPS)-induced septic shock and dextran sodium sulfate (DSS)-induced colitis models. Additionally, we showed that both LPS-induced septic shock and DSS-induced colitis were ameliorated in Gsnor-/- Nlrp3-/- double-knockout (DKO) mice. Mechanistically, GSNOR deficiency increases the S-nitrosation of mitogen-activated protein kinase 14 (MAPK14) at the Cys211 residue and augments MAPK14 kinase activity, thereby promoting Nlrp3 and Il-1β transcription and stimulating NLRP3 inflammasome activity. Our findings suggested that GSNOR is a regulator of the NLRP3 inflammasome and that reducing the level of S-nitrosylated MAPK14 may constitute an effective strategy for alleviating diseases associated with NLRP3-mediated inflammation (Cell Mol Immunol 2024).

Mechanism of arsenic regulation of mitochondrial damage and autophagy induced synaptic damage through SIRT1 and protective effect of melatonin

Xiaoli Zhang（张小莉）, Jing Wang, Shuyuan Li, Kun Chen , Yulan Qiu

School of Public Health, Shanxi Medical University 030001, Xinjian nanlu 56#, Taiyuan, China

**Correspondence email: ylqiu@sxmu.edu.cn*

Abstract

Objectives: Arsenic (As), a widespread environmental pollutant, can induce severe neurological damage worldwide, but the underlying mechanisms remain unclear. Sirtuin 1 (SIRT1) has been reported to exert neuroprotective effects against various neurological diseases by resisting mitochondrial damage and autophagy through deacetylation.

Methods: All the HT22 cells were randomly divided into 9 groups: control, low As (2μM), medium As (4μM), high As (8μM), DMSO, SRT1720 (0.1μM, SRT1720), SRT1720+ high As (0.1μMSRT1720+8μMAs, SRT1720+As), Mel (0.01μM, Mel) and Mel + high As groups (0.01μMMel+8μMAs, Mel+ As).

Result: The levels of SIRT1 in all exposed groups were significantly lower than those in control group. Similarly, the fluorescence intensity of SIRT1 also showed a similar decreasing trend. Cellular and synaptic morphological changes showed that the length of the longest dendrite, the number of primary neurite, and the neurite outgrowth index (NOI)were significantly reduced. The expression levels of C-FOS and α-SYN decreased with increasing $NaAsO_2$ dose. Pathological structural changes also showed that the mitochondrial structure was extremely disturbed and the membrane-like structure of autophagosomes increased. the level of PINK1, Parkin, p62 and LC3B were also obtained. Notably, activator SRT1720 and melatonin (Mel) intervention upregulated SIRT1 and attenuated mitochondrial damage and autophagy, restoring synaptic damage.

Conclusions: As causes neurotoxicity by decreasing SIRT1 production, causing mitochondrial damage and activating autophagy, which provides fundamental data for further study of arsenic neurotoxicity. In addition, blocking this pathway attenuated the synaptic damage of arsenic exposure, which provides a new therapeutic avenue for arsenic neurotoxicity.

Key Words: Arsenic; Mitochondria; Autophagy; SIRT1; Synaptic damage

Phase separation of BRD2 promotes ferritinophagy in depression

ZhenLi（李振）

Shenzhen Hospital of Integrated Chinese and Western Medicine

**Correspondence email:jantqleed@163.com*

Abstract

Background: Depression is a psychiatric disorder with substantial social implications; however, the molecular biological mechanisms that underlie depression are still not fully understood. The atypical phase separation is a mechanism underlying neurological disorders. The interaction between autophagy and iron metabolism plays a critical role in the development of neurological diseases.

Methods: To investigate the pathogenesis of depression, an analysis of super-enhancers (SEs) in the prefrontal cortex of depression model rats was conducted using chromatin immunoprecipitation sequencing (ChIP-seq). We investigated the role of the upstream protein Bromodomain Containing 2 (BRD2) in super-enhancers (SEs) by synthesizing liquid-liquid phase separation proteins in vitro and conducting Fluorescence recovery after photobleaching (FRAP) analysis. Moreover, we investigated the markers of ferritinophagy in cortisol-stimulated primary cortical neuron cells and PC12 cell models to evaluate ferritinophagy in depression models.

Results: Rats exposed to chronic mild stress (CMS) exhibit a reduction in the activation of autophagy-related 7 (ATG7) mediated by super-enhancers (SEs). Ferritinophagy has been documented in rats subjected to chronic mild stress (CMS) and in cellular models of depression. Arid5a initiates the activation of ATG7 through super-enhancers (SEs) and is dependent on the BET family and liquid-liquid phase separation. Dysfunction of ferritinophagy in cellular models of depression is dependent on ATG7. BRD2 exhibits aberrant phase separation in CMS rats. The BET inhibitor JQ1 has shown promise in alleviating depressive behavior in rats subjected to chronic mild stress (CMS).

Conclusions: The ATG7 genes demonstrate activation by super-enhancers (SEs) in both depressed cells and animal models. The increased transcriptional activity of ATG7 has the potential to enhance ferritinophagy. Moreover, the phase separation of BRD2 plays a crucial role in the stimulation of ATG7 via super-enhancers (SEs).

S-nitrosoglutathione reductase alleviates morphine analgesic tolerance by restricting PKCα S-nitrosation

*Ling-Yan Su [1, 3, 4]（苏凌燕）, Lijin Jiao [1, 4], Qianjin Liu [1,, 4], Xinhua Qiao [2, 4], Ting Xie [2], Zhiyu Ma [1], Min Xu [1], Mao-Sen Ye [1], Lu-Xiu Yang [1], Chang Chen [2, *], Yong-Gang Yao [1, *]*

[1] Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, Yunnan 650204, China
[2] Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China
[3] Yunnan Agricultural University, Kunming, Yunnan 650201, China
[4] These authors contributed equally to this work

**Correspondence email: yaoyg@mail.kiz.ac.cn;changchen@moon.ibp.ac.cn*

Abstract

Morphine, a typical opiate, is widely used for controlling pain but can lead to various side effects with long-term use, including addiction, analgesic tolerance, and hyperalgesia. At present, however, the mechanisms underlying the development of morphine analgesic tolerance are not fully understood. This tolerance is influenced by various opioid receptor and kinase protein modifications, such as phosphorylation and ubiquitination. Here, we established a murine morphine tolerance model to investigate whether and how *S*-nitrosoglutathione reductase (GSNOR) is involved in morphine tolerance. Repeated administration of morphine resulted in the down-regulation of GSNOR, which increased excessive total protein *S*-nitrosation in the prefrontal cortex. Knockout or chemical inhibition of GSNOR promoted the development of morphine analgesic tolerance and neuron-specific overexpression of GSNOR alleviated morphine analgesic tolerance. Mechanistically, GSNOR deficiency enhanced *S*-nitrosation of cellular protein kinase alpha (PKCα) at the Cys78 and Cys132 sites, leading to inhibition of PKCα kinase activity, which ultimately promoted the development of morphine analgesic tolerance. Our study highlighted the significant role of GSNOR as a key regulator of PKCα *S*-nitrosation and its involvement in morphine analgesic tolerance, thus providing a potential therapeutic target for morphine tolerance.

Key Words: analgesic tolerance, morphine, PKCα, GSNOR, *S*-nitrosation

Fecal microbe transplantation ameliorates arsenic-and-fluoride-induced nephrotoxicity of offspring rats co-exposure to arsenic and fluoride through microbiota-gut-kidney axis

Xiaolin Tian[1]（田晓琳）, *Xiaoyan Yan*[*]

School of Public Health, Shanxi Medical University, Taiyuan 030001, Shanxi

Correspondence email: tianxiaolin@sxmu.edu.cn1, yanxiaoyan@sxmu.edu.cn

Abstract

Background Co-contamination of arsenic (As) and fluoride (F) is widely distributed in groundwater, which are known risk factors for the nephrotoxicity. Emerging evidence has linked environmentally associated nephrotoxicity with the disturbance of gut microbiota and blood metabolites.

Methods On the one hand, we established an animal model of male kidney injury caused by alone and combined exposure of arsenic and fluoride in rats to investigate the regulatory effect in intestinal flora and blood metabolism and its nephrotoxicity. On the other hand, we also established the rat model through the fecal microbiota transplantation (FMT) to comprehensive investigated the key regulatory role of gut microbiota in kidney injury.

Results The results showed that arsenic and fluoride exposure significantly increased creatinine level and caused the damage of kidney structure. In addition, arsenic and fluoride disrupted the intestinal barrier which was manifested as the decreased protein expression of ZO-1 and Occludin. Multiple altered gut bacterial microbiota at phylum and genus levels after arsenic and fluoride exposure. The metabolome data showed that arsenic and fluoride exposure remarkably altered the serum metabolites associated with the tryptophan metabolism and phenylalanine metabolism pathway, with hippuric acid level significantly enhanced in all exposed. On the contrary, FMT effectively alleviated intestinal and kidney injury. Remarkably, lactobacillus was decreased significantly in exposed group, however, its abundance was remarkably enhanced through fecal microbiota transplantation. Besides, hippuric acid, a harmful biomarker of gut-kidney axis, significantly deceased after FMT.

Conclusions In conclusion, FMT effectively alleviated intestinal injury, reshaped the composition of intestinal microflora and circulating metabolites, slowed down the accumulation of harmful metabolites in the gut-kidney circulation, and finally ameliorated the toxic injury of kidney to a certain degree.

Key Words: arsenic; fluoride; nephrotoxicity; fecal bacteria transplantation

Metabolic reprogramming in placental mitochondria respiration contributes to the reproductive success of indigenous Tibetan women living at high altitude

Cuomao Niangji[1]*（娘吉措毛）*, *Huifang Liu*[1], *Tana Wuren*[1,2,*]

[1] *Research Center for High Altitude Medicine, School of Medicine, Qinghai University, Xining 810001, China;*
[2] *Key Laboratory for Application of High-Altitude Medicine, Qinghai University, Xining 810001, China*

**Correspondence email: tana.wuren@qhu.edu.cn*

Abstract

Tibetans, who have resided at high altitudes for thousands of years, have adapted to the challenges of the hypobaric hypoxic environment, evidenced in part by their ability to successfully reproduce in such extreme environmental conditions. Stereological studies revealed that placentas from Tibetans residing at 3780 m (HT) had higher placental efficiency (birthweight to placental weight ratio) and greater anatomical capacity for oxygen diffusion than European-descent living at 3100 m. Hypoxic ischemic conditions from labor were associated with higher mitochondrial fission protein DRP1 in lower altitude (2200 m) Tibetan and Han placentas (LT, LH) compared to HT. In contrast, HT exhibited higher fission protein DRP1, and morphology indicated mitochondrial fission, corresponding to a less stressed state. Accordingly, HT had fewer mitochondria and more respiratory complexes than LT and LH. Lower altitude placenta had elevated TID1 and lower CLPP, indicative of mitochondrial stress as well as elevated rough endoplasmic reticulum stress proteins phosphorylated eIF2α (P-eIF2α), ATF4, ATF6, and XBP1 compared to HT. placentas from high-altitude Tibetan pregnancies have optimized morphology for oxygen diffusion and show evidence of greater mitochondrial efficiency and blunted response to hypoxic stress compared to placentas from lower-altitude Tibetan and Han pregnancies.

Key Words: Tibetan, plateau adaptation, placenta, mitochondria, endoplasmic reticulum，Redox Biology

Ganoderma Lucidum Spore Lehuo Powder Attenuates Experimental Autoimmune Encephalomyelitis by Modulating Microglial Activation and Polarization through the NF-κB Signaling Pathway

*Lu Zhang[1 †], Jie Chen[1,2†], Sauchu Yuen[1], Wenting Li[1], Meiling Wu[1], Jiangang Shen[1,3]**

1 School of Chinese Medicine, LKS Faculty of Medicine, the University of Hong Kong. Hong Kong, China
2 Department of Orthopedics, Shanghai Institute of Traumatology and Orthopedics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, of China
3 Shenzhen Institute of Research and Innovation, The University of Hong Kong, Shenzhen, China

**Correspondence email: zhanglu9@connect.hku.hk*

Abstract

Multiple Sclerosis (MS) is a debilitating neurodegenerative disease affecting the central nervous system (CNS), for which an effective therapeutic strategy remains elusive. This study investigates the potential of Ganoderma Lucidum Spore Lehuo (GLS) powder, a natural product derived from Ganoderma, as a novel therapeutic agent for MS. Using an experimental autoimmune encephalomyelitis (EAE) mouse model, the study tested the hypothesis that GLS could mitigate MS pathology by inhibiting microglial activation and promoting an anti-inflammatory M2-like phenotype. The results demonstrated that GLS treatment effectively ameliorated disease severity, reduced inflammatory infiltration and demyelination, and modulated microglial activation and polarization in the spinal cord.

Further in vitro experiments revealed that GLS could suppress the nuclear factor-κB (NF-κB) signaling pathway, thereby reducing the release of reactive nitrogen species (RNS) by microglia. Additionally, the in vitro studies on microglia and neuronal cells showed that GLS exerts protective effects on neurons.

Collectively, these findings suggest that GLS has therapeutic potential for treating EAE/MS by attenuating microglial activation and polarization, leading to anti-inflammatory, anti-oxidative effects, and inhibiting microglial-mediated neuronal death. This study provides a promising avenue for the development of a novel therapeutic agent for Multiple Sclerosis.

Brain-targeted biomimetic liposomes with neuroprotective effects for precise therapy of ischemic stroke

Siyu Tian（田丝雨）, Yan-Zhong Chang

Hebei normal university, 050024, 20 South Second Ring Road East, Shijiazhuang province, China;

**Correspondence email: tiansiyu9615@163.com*

Abstract

Stroke is a major cause of morbidity and mortality in both developing and developed countries. After thrombolysis, the level of oxidative stress and excessive accumulation of iron in the brain injury area increased rapidly, resulting in a large number of neural cells apoptosis and ferroptosis. Moreover, due to the influence of the blood-brain barrier, most drugs cannot effectively reach the injured area for a long time to treat the neurons with lesions. Based on the effect of platelet targeting on endothelial injury and the penetration of rabies virus polypeptide blood-brain barrier, liposomes loaded with natural antioxidant lycopene and iron chelating agent deferoxamine with ROS response were designed. After treatment with nanomaterials, the brain injury area of ischemia-reperfusion mice can be significantly reduced, and the apoptosis and ferroptosis of brain cells can be improved. This approach provides a new multifunctional approach for the treatment of stroke, and also provides a new strategy for similar nerve ischemia or peripheral ischemia.

Inorganic Nanosensitizers for Cancer Nanodynamic Therapy

Xiaoyan Zhong,[a,b] （仲晓燕） Yan An,[a] and Xiangliang Yang [b]

[a] Department of Toxicology, School of Public Health, Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, MOE Key Laboratory of Geriatric Diseases and Immunology, Suzhou Medical College of Soochow University, Suzhou, Jiangsu 215123, China

[b]National Research Centre for Nanomedicine, College of Life Science and Technology, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China

**Correspondence email: xyzhong@suda.edu.cn, yangxl@hust.edu.cn*

Abstract

Trends in nanodynamic therapy (NDT) that precisely regulates in-situ reactive oxygen species (ROS) generation within tumors have stimulated greater research efforts toward the development of novel nanosensitizers due to their eminent roles in increasing ROS. In this talk, I will focus on the development of high-efficiency, and low-toxicity nanosensitizers, and propose a few research works where the designed nanosensitizers, including clinical X-ray responsive photosensitizer, ultrasound (US) responsive sonosensitizers with tumor microenvironment (TME) modulation capacities, can be used for radiodynamic therapy, sonodynamic therapy, and chemodynamic therapy of cancer, respectively, which would provide the reserves of nanosensitizers and might open up new opportunities for advanced oncotherapy.

Nano-assemblies overcome cancer multidrug resistance for effectively synergistic chemo-immuno-oncotherapy

Yingnan Liu[1,2,3,*]*（刘英楠）*, *Su Li*[1,2,3], *Guofang Zhang*[2,3], *Yang Li*[2,3,*]

[1]*Division of Allergy & Immunology, Department of Biosciences & Medical Biology, Paris Lodron University of Salzburg, 5020 Salzburg, Austria.*
[2]*Laboratory of Inflammation and Vaccines, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, Guangdong, China.*
[3]*Laboratory of Immunology and Nanomedicine & China-Italy Joint Laboratory of Pharmacobiotechnology for Medical Immunomodulation, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, 518055 Shenzhen, China.*

**Correspondence email: yn.liu1@siat.ac.cn; yang.li@siat.ac.cn*

Abstract

Cancer, as one of the most devastating diseases, is causing millions of deaths worldwide annually. Chemotherapy remains the most commonly used therapeutic strategy in clinics. Among various chemo-drugs, doxorubicin (DOX) is the most used chemo-drugs in clinic, which exhibits anti-tumor capacity by generating reactive oxygen species (ROS) in cancer therapy. However, the long-term administration of drugs lead to the chemo-drug resistance, which bring the major challenge for developing effective onco-therapeutics. For instance, the resistance to intracellular ROS generated by DOX has raised considerable attention for cancer therapy. Many studies have revealed that the intracellular glutathione (GSH), an antioxidant molecule, could regulate intracellular oxidative stress defense as a ROS-scavenging agent in drug-resistant tumor cells. Thus, the modulation of redox balance would be an important attempt to synergize with chemo-drugs, such as DOX, which it is critical to reduce drug resistance of chemo-drugs for effective oncotherapy.

Here, to reverse suppressive tumor microenvironment (TME) and overcome the MDR for effective tumor killing, the nano-assemblies are developed for tumor chemo-immunotherapy. The delivery system could not only induce the immunogenic tumor cell death but also weaken the anti-ROS capacity of tumors from the reducing the cancer′ s MDR. On the other hand, to enhance antigen presentation and T cell activation, the adjuvant is used to activate the immune responses. In B16F10 and MCF-7 tumor models, the results indicated that the designed nano-assemblies showed the powerful anti-tumor effects by overcoming MDR, killing cancer and TAMs cells, and promoting the infiltration and activation of CD8+ T cells eventually. To summarize, our research provides a nanoplatform to overcome MDR, and to simultaneously activate the immune cells and enhance chemotherapy for effective anti-tumor chemo-immunotherapy.

Key Words: Reactive Oxygen Species, Redox Biology, Chemo-Immunotherapy, Tumor Microenvironment, Multidrug Resistance

Nanomaterials for tumor-cell-specific catalytic therapy

Xi Hu[1]（胡希）, Fangyuan Li,[2] Daishun Ling[3]

[1] School of Pharmacy, Anhui Province Key Laboratory of Pharmaceutical Preparation Technology and Application, Anhui University of Chinese Medicine, Hefei, Anhui 230038, China.
[2] Songjiang Hospital and Songjiang Research Institute, Shanghai Key Laboratory of Emotions and Affective Disorders, Shanghai Jiao Tong University School of Medicine, Shanghai 201600, China.
[3] Frontiers Science Center for Transformative Molecules, School of Chemistry and Chemical Engineering, National Center for Translational Medicine, Shanghai Jiao Tong University, Shanghai 200240, China.

**Correspondence email: huxi@ahtcm.edu.cn ;dsling@sjtu.edu.cn ;lfy@zju.edu.cn*

Abstract

Functional metal nanomaterials with unique physical and chemical properties have been widely utilized to mediate redox catalysis for cancer treatment. However, a significant challenge in the application of these metal nanomaterials in precision oncology lies in accurately controlling their biological performance within complex in vivo microenvironments, that is, exerting antitumor activity exclusively within tumor tissues while remaining biocompatible and non-toxic to normal tissues. We precisely tailor the coordination environment of metal atoms and metal-ligand interactions to develop a series of stimuli-responsive allosteric antitumor nanomaterials. These nanomaterials are designed to initiate atomic-scale allosteric responses when exposed to endogenous stimuli within the tumor microenvironment (such as pH, ROS, etc.) and/or exogenous stimuli (such as near-infrared light), thereby selectively activating antitumor activity for tumor cell-specific catalytic therapy. Furthermore, we focus on the abnormal metabolism and key metabolic enzymes in tumors. By selectively regulating the catalytic activity of metabolic enzymes and accurately mimicking the conformations of their cofactors, we precisely reprogram metabolic behaviors within tumor cells and the metabolic communication between tumor cells and immune cells, thus achieving tumor cell-specific metabolic immunotherapy. We aim to selectively regulate tumor-specific abnormal metabolism, DNA damage repair, and immune responses across multiple levels—including molecular, organelle, cellular, and tumor tissue levels—thereby paving the way for precise and targeted tumor therapy.

Key Words: Nanomaterials; Redox Catalysis; Atomic-Level Modulation; Metabolic Modulation; Tumor-Cell Specific Therapy

Nanomedicine by Modulating ROS for Oncotherapy

Guofang Zhang[1,2*]（张国芳）, *Yingnan Liu*[1,2,3,], *Yang Li*[1,2,*]

[1]*Laboratory of Inflammation and Vaccines, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, Guangdong, China.*
[2]*Laboratory of Immunology and Nanomedicine & China-Italy Joint Laboratory of Pharmacobiotechnology for Medical Immunomodulation, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, 518055 Shenzhen, China.*
[3]*Division of Allergy & Immunology, Department of Biosciences & Medical Biology, Paris Lodron University of Salzburg, 5020 Salzburg, Austria.*

**Correspondence email: gf.zhang@siat.ac.cn; yang.li@siat.ac.cn*

Abstract

The reactive oxygen species (ROS) plays an important role in cancer therapy. ROS plays a promoting role in the occurrence and development of tumors. Various stimulates (such as stress, tobacco, environmental pollutants, radiation, viral infection, etc.) can promote the survival, proliferation and metastasis of tumor cells by generating ROS. While, excess ROS can activate the cell death pathways (such as apoptosis, necrosis, and autophagy), thereby limiting cancer progression. Thus, modulating of ROS balance is vital for oncotherapy.

Chemotherapy and tumour immunotherapy remain the most commonly used therapeutic strategy in clinics. The intracellular ROS accumulation can increase or reduce the tumour immunotherapy effects, while a continuous ROS stimulation by chemo-drugs in tumor can cause chemo drug-resistant. By modulating the ROS, we designed a serious of nanodrugs for effective chemotherapy and chemo-immunotherapy. The designed nanodrugs could be targeting accumulated in tumor to reduce the systematic side effects, but also be used to deliver the antioxidant-scavenging agent into the tumor microenvironment (TME) to improve the ROS level and reduce drug resistance for effective chemotherapeutics. In the other hand, a TME-responsive nanodrug has also been designed to reverse the suppressive TME by promoting the infiltration and activation of $CD8^+$ T cells and eventually to achieve an effective anti-tumor chemo-immunotherapy. By precisely modulating ROS levels in tumors, our designed nanodrugs achieved effective onco-therapeutic effects.

Key Words: Reactive Oxygen Species, Chemo-Immunotherapy, Tumor Microenvironment, Nanomedicine

Protective effect of platinum nano-antioxidant and nitric oxide against hepatic ischemia-reperfusion injury

Jing Mu（穆婧）

Peking University Shenzhen Hospital

**Correspondence email: jing.mu@pkuszh.com*

Abstract

Specific therapeutic interventions of hepatic ischemia-reperfusion injury (IRI) to attenuate liver dysfunction or multiple organ failure following liver surgery and transplantation remain a key concern. Here we present an innovative strategy by integrating a platinum nanoantioxidant and nitric oxide synthase (iNOS) into the zeolitic imidazolate framework-8 (ZIF-8)-based hybrid nanoreactor for effective prevention of IRI. Platinum nanoantioxidant could scavenge excessive reactive oxygen species (ROS) at the injury site and meanwhile generate oxygen for subsequent synthesis of nitric oxide (NO) under the catalysis of iNOS. Such cascade reaction successfully achieved dual protection for the liver through ROS clearance and NO regulation, remarkably enabling reduction of oxidative stress, inhibition of macrophage activation and neutrophil recruitment, and ensuing suppression of proinflammatory cytokines. The current work establishes a proof of concept of multifunctional nanotherapeutics against IRI, which may provide a promising intervention solution in clinical use.

Disruption of circadian rhythms promotes ventricular arrhythmia via oxidative stress and electrocardiography alternation.

Bingping Yang,(杨冰萍) Bin Liu, Zhen Wang.

Shantou University medical college.515000

**Correspondence email: 22bpyang@stu.edu.cn*

Abstract

The circadian clock plays a central role in many aspects of cardiac physiology. Disruption of circadian rhythm (DCH) with jet-lag, shift work, etc. increases the risk of cardiac arrhythmia. However, the impact of DCH on cardiac electrophysiology, Ca^{2+} handling, and especially fetal ventricular tachycardia/fibrillation (VT/VF) is unknown.

To investigate the effect of DCH on ventricular arrhythmia, 12-week Sprague-Dawley rats were kept in a 12-h light:12-h dark environment (control group) or exposed to an 8-h phase advance of the light cycle every two days (experimental group) for 10 days. Rat hearts were langendorff perfused and optical mapped at 7-Hz pacing frequency, in which epicardium membrane potential and Ca^{2+} were visualized with potential and Ca^{2+} sensitive dyes separately.

Circadian rhythm disruption prolonged the action potential duration (APD) or Ca^{2+} transient duration (CaTD). In addition, the conduction velocity (CV) was slower in the experimental group. Prolonged APD and slow CV are risk factors for ventricular arrhythmia. Indeed, the DCH group tends to have more susceptibility to VT/VF during ischemia-reperfusion. Transcriptome analysis was used to screen the genes expressed alternatively with DCH. Among the genes tested, 15 were enriched in at least four oxidative stress-related signaling pathways. Western blot confirms that CX43, the key factor regulating CV, was decreased after DCH. Interestingly, the expression of CX43 is proposed to be affected by oxidative stress in the literature.

Conclusion: Disruption of normal circadian rhythm prolonged the APD and decreased the CV of the heart. These are probably achieved via the induction of oxidative stress, followed by a reduction of CX43. The APD prolongation and CV slowing down together may contribute to the increased susceptibility to ventricular arrhythmia after DCH.

Chrysanthemolide J mitigates acetaminophen-induced hepatotoxicity through LKB1 and PP2A-mediated mitochondrial hormesis

Fei Zhou [a,‡] (周飞), *Yu Liu* [a,‡], *Qing-Wen Zhang* [a, b,*], *Li-Gen Lin* [a, b,*]

[a] *State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Avenida da Universidade, Taipa, Macao 999078, China*
[b] *Department of Pharmaceutical Sciences, Faculty of Health Sciences, University of Macau, Avenida de Universidade, Taipa, Macao 999078, China*

**Correspondence email: Qing-Wen Zhang (qwzhang@um.edu.mo); Li-Gen Lin (ligenl@um.edu.mo).*

Abstract

Hormesis is an adaptive response of organisms to moderate stressors, characterized by a biphasic dose response featuring low-dose stimulation and high-dose inhibition. The hormetic effect is crucial in determining the clinical dosage, while the underlying mechanism remains uncertain. Acetaminophen (APAP) possesses analgesic and antipyretic properties; nonetheless, an overdose may result in hepatotoxicity and acute liver failure. The flower of *Chrysanthemum indicum* is an edible-medicinal herb with the traditional effect of hepatoprotection, but its active principles remain unclear. The current study showed that chrysanthemolide J (CJ), a new compound isolated from the flowers of *C. indicum*, alleviated APAP-induced hepatotoxicity in AML12 hepatocytes (0.156, 0.625, and 2.5 μM) and mice models (0.3125, 1.25, and 5 mg/Kg). Interestingly, the hepatoprotective effects of 2.5 μM and 5 mg/Kg were weaker than those of 0.625 μM and 1.25 mg/Kg, indicating the hormetic effect. AMP-activated protein kinase (AMPK) is a key regulator of energy metabolism homeostasis and plays an important role in the adaptive response process. The hormetic effect of CJ was verified through promoting AMPK-mediated mitochondrial biogenesis and mitophagy, while inhibiting AMPK-mediated mitochondrial oxidative stress. CJ directly bound to liver kinase B1 (LKB1) and protein phosphatase 2 (PP2A) with the Kd values of 1.24 ± 0.22 and 7.19 ± 1.58 μM, respectively. CJ initiated binding to the LKB1 at 0.156 μM with high affinity. As the dosage increased, LKB1 activity saturated at 0.625 μM before binding to PP2A at 2.5 μM, resulting in a decline in AMPK activity at 2.5 μM and leading to a reduced hepatoprotective effect against APAP. Taken together, our findings suggested that CJ may have the potential in treating APAP-injured liver injury, and the hormetic effect offers direction for future dosage strategies.

Network Medicine landscape on the Health-Enhancing Properties of Natural Antioxidants

Mengchen Liu（刘梦晨）

Zhuhai campus of Zunyi Medical University

**Correspondence email: 2731382028@qq.com*

Abstract

Natural antioxidants have attracted increasing attention for their potential in promoting health and preventing disease, yet the mechanisms underlying their redox activities, and their protective effects remain incompletely understood. Network medicine, an emerging field that analyzes complex molecular interactions, offers a promising framework for uncovering how these compounds function at a systems level. However, a gap exists in integrating network medicine with the study of natural antioxidants, particularly in understanding the molecular networks involved. This study addresses this gap by employing a network-based approach to investigate the interactions between natural antioxidant compounds and key regulatory nodes within biological signaling networks. We focus on the role of these interactions in maintaining cellular redox balance and mitigating the progression of chronic diseases associated with oxidative stress. Our analysis identifies specific compounds, including quercetin, palmitic acid, and linoleic acid, present in camellia oil, which modulate critical metabolic pathways related to phospholipids, fatty acids, and bile acids. These findings demonstrate the potential of network medicine to uncover novel antioxidant therapies and elucidate the molecular mechanisms that confer protection against tissue injury caused by oxidative stress. This study highlights the critical role of network medicine in advancing the understanding of natural antioxidants. Furthermore, it advocates for the integration of comprehensive evaluation criteria including chemical composition analysis, bioactivity assays, and animal study to assess the safety and efficacy of these compounds as health supplements. By bridging the gap between molecular insights and therapeutic applications, our study contributes to the development of innovative strategies for health promotion.

Keyword： antioxidant, natural product, network medicine, health promotion

Osteoprotective and osteoblastic potential of the Sambucus javanica Reinw ex Blume subsp. javanica leave

Treethip Sukkho, Young-Joon SURH, Chartchai Khanongnuch, Saisamorn Lumyong, Jetsada Ruangsuriya, Thanawat Pattananandecha, Sutasinee Apichai, and Chalermpong Saenjum

Section of Pharmaceutical Biotechnology, Department of Biotechnology, Multidisciplinary and Interdisciplinary School, Chiang Mai University, Chiang Mai, Thailand

**Correspondence email: Treethip.sk@gmail.com*

Abstract

Sambucus javanica subsp. *javanica* (SJ) has been used in the traditional medicine of People-Forest-Miang communities of Thailand for healing bone fractures. In the present study, we investigated the potential of the crude extracts and fractions obtained from the leaf parts of SJ for osteoporotic protection in the murine preosteoblast MC3T3-E1 cell line. We found that the crude water and ethanolic extracts stimulated osteoblastic cell proliferation and enhanced osteoprotective/osteoblastic activity, as measured by alkaline phosphatase activity, expression of osteocalcin (OC) and osteoprotegerin (OPG), and the OPG/the receptor activator of nuclear factor-κB ligand (RANKL) ratio. Additionally, they exhibit a negative impact on bone resorption by reducing RANKL expression and inhibit production of reactive oxygen species. Additionally, major and minor active compounds found in both extracts have been documented to enhance bone formation and inhibit bone resorption. Therefore, our findings present novel evidence indicating that the SJ crude extract could be further utilized as a formulation for the development of bone health products.

Key Words: *Sambucus javanica* subsp. *javanica*, Osteoblastic functional enhancing activity, People-Forest-Miang, Receptor activator of nuclear factor-κB ligand (RANKL), Redox Biology, Reactive oxygen species (ROS)

Design, synthesis and antiparasitic activity of a novel naphthoquinone molecule based on SjTGR from Schistosoma Japonicum

Tingyi Yin[1]（殷婷怡）, Jiankang Liu[1,2,3], Yan Zheng[1*],

[1] *Department of Dermatology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China;*

[2] *Center for Mitochondrial Biology and Medicine, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, Xi'an Jiaotong University.*

[3] *School of Health and Life Sciences, University of Health and Rehabilitation Sciences, Qingdao 266071, China*

**Correspondence email: zenyan66@126.com*

Abstract

Atopic Dermatitis (AD) is a prevalent inflammatory skin disease that is currently incurable. Plasma-activated solutions (PAS) (e.g., culture media, water, or normal saline, previously exposed to plasma) are being studied as novel therapy. Recently, PAS is gaining attention due to its advantages over cold atmospheric plasma. Thus we explore the application of PAS in treating AD. Our work demonstrated that PAS significantly alleviated AD-like symptoms. These therapeutic effects of PAS on AD mice were associated with the downregulation of tissue reactive oxygen species (ROS) levels and the activation of the antioxidant molecule Nrf2. In vitro experiments revealed that PAS could decrease ROS level and regulate cytokine expression. Additionally, PAS could upregulate the expression of antioxidant stress molecules such as Nrf2, HO-1 and NQO1 in keratinocytes. Overall, PAS demonstrated potent therapeutic potential for AD without notable side effects. Our research provided a promising approach to AD treatment and may open a novel avenue for treating such skin diseases and setting a novel medical scenario feasible for applying PAS.

An in vitro assessment of Redox-stress Response Capacity (RRC)

Li Shilong[1,2]（李世龙）,Jiao Meng[1],Chen Chang[1,*]

[1] *Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China*
[2]*Unicersity of Chinese Academy of Sciences, Beijing 100049, China*

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Background: Redox regulation is closely associated with various physiological processes, including aging. We proposed “redox-stress response capacity (RRC)” as a new concept in our previous work (Redox Biology, 2017), and found that the decline in RRC was a dynamic characteristic of aging. Some studies have begun to use the decline in RRC as an indicator to evaluate aging. However, there is currently a lack of straightforward and convenient methods for evaluating RRC. While exploring the mechanism underlying the decline in RRC, we identified peroxiredoxin 2 (PRDX2) as a redox signal sensor (Sci China Life Sci, 2023). The irreversible overoxidation of PRDX2 during aging results in losing its ability to form disulfide bonds to transmit redox signals.

Method: Thioredoxin 1 (Trx1) can recognize and reduce the intermolecular disulfide bonds formed by PRDX2. By conjugating Trx1 with the redox-sensitive fluorescence protein roGFP2, we can convert the disulfide bond signal into a detectable fluorescent signal.

Results: Overexpressing the Trx1-roGFP2 fusion protein as a probe in human dermal fibroblasts (HDFs), the probe responds well to H2O2 in young cells but shows no significant response in aging cells, which is consistent with the decline in RRC. We purified the Trx1-roGFP2 probe through prokaryotic expression and validated its response capability in vitro. The probe does not respond to H2O2 and GSSG signals by itself; however, it can respond to low concentrations of H2O2 in the presence of PRDX2 protein or cell lysates.

Conclusion: In summary, we have developed a new strategy for in vitro detection and evaluation of RRC based on the Trx1-roGFP2 probe that responds to PRDX2 disulfide bond formation signals. The detection of dynamic changes in signal response, as opposed to the static detection of small molecules, better reflects the body's RRC and offers a new approach for future testing of biological tissue samples (e.g., blood, urine).

Key Words: Redox-stress Response Capacity; Trx1; fluorescence probe

Construction of the platform for precision redox detection and regulation

Minghao Deng [1]（邓明昊）, Jiarui Wang[1], Chang Chen[1,2*]

[1]*Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China*

[2]*University of Chinese Academy of Sciences, Beijing 100049.*

**Correspondence email: changchen@moon.ibp.ac.cn*

Abstract

Background: Redox regulation governs many important physiological and pathological processes. However, most studies of redox regulation are at global level. Based on the 5R principles of precision redox, we need to specifically study redox regulation at the organelle level. Therefore, it is necessary to construct a research platform for precise detection and regulation of cellular redox states.

Methods: To construct a precise redox detection platform, we expressed the HyPer4 probe for H_2O_2 and the Grx1-roGFP2 probe for GSH/GSSG in different organelles in 293T cells and C. elegans. To construct a precise redox regulation platform, we combined the BRET-based LuminON system to overexpress redox enzymes localized to different organelles via optogenetic approaches.

Results: Precision redox detection platform: We construct stable 293T cell lines expressing HyPer4 and Grx1-roGFP2 probes localized at the cytoplasm, mitochondria, nucleus, and endoplasmic reticulum, as well as *C.* elegans strains expressing probes in body wall muscle and neuronal cells. The localization and response of the probes in different organelles have been verified, which means the platform can be used to detect cellular redox levels under various physiological or stress conditions.

Precision redox regulation platform: We constructed cell lines to overexpress $PRDX2_{Cyto}$, $SOD2_{mito}$, and CAT_{ER} via optogenetic approaches, with BRET-based LuminON system and redox regulation has been validated. By controlling the duration of blue light exposure, we can achieve the precise regulation of redox at the level of organelle.

Significance: Through construction of the platform mentioned above, we can achieve precise detection and regulation of redox at the organelle level. This study provides useful tools for future research in the field of precision redox.

Key Words: redox platform, precision redox detection and regulation

Effect of electrolytic water generated by an alkaline ionizer on the concentration change of kelp extract

Takuma Sato[1 3], Koji Fukui[1], Mamoru Kaneko[1], Nobuyasu Hiramatsu[2]

[1] *Shibaura Institute of Technology*

[2] *Fukuoka university*

[3] *Panasonic*

**Correspondence email: nb24101@sic.shibaura-it.ac.jp*

Abstract

Introduction: It is well known that components in food solutions dissolve in higher concentrations when heated or pressurized than when extracted with water. They are two mainly two methods for making kelp stock: short-time heating and long-time water-extraction. In Japan, AEW is known to be effective not only in improving gastrointestinal symptoms, but also known in enhancing the extraction of umami compounds from food ingredients. By electrolyzing tap water, hydrogen-containing AEW is produced through a reduction reaction at the cathode, and acidic water is produced through an oxidation reaction at the anode.

Experiment: The electrolytic water was generated by a Panasonic alkaline ionizer. A given weight of kelp was treated to high pressure treatment in 2 mL of water. They were then the amount of each component was quantified by high performance liquid chromatography. Changes in the kelp's cell structure were then observed using an electron microscope.

Results and Discussion: As shown in the figure, the concentration of glutamic acid was higher in kelp soaked in AEW with a pH of 10 for 15 min than in kelp immersed in tap water with a pH of 7.2 for 60 min under a pressure of 0.1 MPa.

AEW was found to be able to extract glutamic acid from kelp in a soaking time that was a quarter time required with tap water. We plan to provide detailed information on changes in glutamic acid concentration and the changes in the kelp cell structure at the presentation.

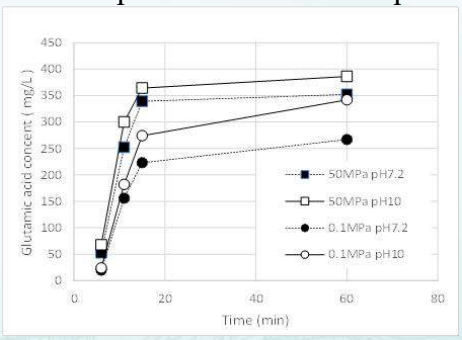


Fig. Time dependence of glutamic acid extraction under high pressure (20mg/2mL (Kelp/water))

Exploring the Precision Redox Map of Cells and C. elegans under Different Treatment Conditions with High Glucose

Yuyunfei Huang[1]（黄雨云飞）, Dongli Wu[1], Xinghua Qiao[2], Chang Chen[2*]

[1] *College of Life Science, University of Chinese Academy of Sciences, Beijing, China. 100049*

[2] *National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China. 100101*

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Background & Aim: Glucose is one of the important energy sources for physiological activities, but high glucose concentration environment can cause cell damage, which is called glucotoxicity. Redox stress is considered one of the mechanisms by which glucotoxicity causes cell damage. Current researches on the redox states of cells under high glucose conditions is mostly global and general. We aim to accurately depict the precise redox map of different organelles under high glucose stimulation.

Methods: To accurately monitor the changes in cellular redox state under high glucose stimulation, genetically encoded fluorescent probe HyPer4(H_2O_2-specific) and Grx1-roGFP2(GSH/GSSG-specific) were expressed in living cells, and located to different organelles. Then the cells were treated under glucose concentrations from 0 to 100 mM, and different stimulating time from 0 to 24 hours. To achieve real-time in vivo observation of the changes in redox states of C. elegans, probes were expressed in neurons and body-wall muscle tissues of C. elegans, locating to cytoplasm, mitochondria, nucleus, and endoplasmic reticulum, respectively. Then a microfluidic device combined with laser confocal microscopy system was built for real-time precise detection of the redox state of C. elegans and cells under short term (within 1 hour) high glucose stimulation.

Results: 8 stable cell lines and 16 C. elegans lines were constructed, specifically expressing probes in 4 organelles and 2 types of tissue in C. elegans. As the glucose concentration of glucose raised, the level of H_2O_2 increased in endoplasmic reticulum, while decrease in cytoplasm, exhibiting an opposite trend in GSSG/GSH level. During the treatment of high glucose, the level of H_2O_2 increased and decreased in cytoplasm, while the GSSG/GSH level decreased in endoplasmic reticulum and increased in cytoplasm. Among all the treatments above, the levels of H_2O_2 and GSSG/GSH remained unchanged in nucleus and mitochondria. In real-time high glucose stimulation, the levels of H_2O_2 and GSSG/GSH in the cytoplasm experienced an increase followed by a decrease, while the level of H_2O_2 in endoplasmic reticulum decreased rapidly after the stimulation. In the body-wall muscle tissue of C. elegans, the level of H_2O_2 in endoplasmic reticulum decreased in a short time after high glucose stimulation.

Conclusion & Significance: We found that H_2O_2 level in endoplasmic reticulum changes first under high glucose stimulation. The trends of H_2O_2 and GSSG/GSH level changes in cytoplasm are the opposite with it in endoplasmic reticulum. We attempt to reconfirm these redox changes on C. elegans in the future work.

Key Words: High Glucose, H_2O_2, GSH, genetically encoded fluorescent probe, redox map

Improvement of mouse bone marrow transplantation and chimerism analysis by qPCR of the modified gene

Gang Yu*（余钢），Xijian Chen，Jinwei Guo，Jiahui Ge，Yingbi Zhou，Bin Liu

Cardiovascular Research Center, Shantou University Medical College, Shantou 515041, China

**Correspondence email:rufusyg@stu.edu.cn*

Abstract

Background: Bone marrow transplant models have been used by more and more researchers to study the functions of genes in hematopoietic or immune cells. However, there are still some problems such as poor reproducibility and low survival rate after transplantation to establish a chimeric mouse model with bone marrow transplantation. Furthermore, existing methods using flow cytometry or qPCR technology are unable to directly and accurately calculate the chimerism rate of a certain BM transplantation experiment.

Methods: WT, Ep3-/-, Cox-1-/- and ROSAmT/mG mice were used. The survival rates of mice after bone marrow transplantation (2 irradiations [4.0 Gy each time] with a 6 h interval or one irradiation at a dose of 8.0 Gy) were recorded. The chimeric rates were calculated by using real-time fluorescence quantitative PCR by using DNAs extracted from the blood with primers to amplify the corresponding modified allele or obtained by utilizing flow cytometry. Chimerism was also verified in mice transplanted with ROSAmT/mG bone marrow by fluorescence microscopy.

Results: The survival rate of mice was higher when the mice were irradiated twice with lower irradiation dose compared with that of single irradiation. ($P < 0.05$). The mice recovered well after two months of bone marrow transplantation. The chimeric rate[WTBM-Ep3KO (87.2 ± 2.90) %, Ep3KO BM-WT (93.32 ± 0.89) %, WTBM-Cox-1KO (91.83 ± 1.78) %, WTBM-mT/mG (89.24 ± 1.64) %] of bone marrow transplantation detected by qPCR using primers to amplify the corresponding modified allele such as that of Ep3-/- or Cox-1-/- was without difference versus that obtained by using flow cytometry（91.2±1.17）%. It was also not different from that calculated by qPCR (95.77±0.52) % of a donor male gene in the blood of the recipient female mice as reported in the literature.

Conclusion: We establish a convenient and reliable real-time quantitative PCR (qPCR) method for detection of chimerism rate of genetically modified mouse bone marrow transplantation, in order to facilitate the study of cardiovascular and inflammatory diseases.

Key Words: Bone marrow transplantation, gene modification, chimerism rate, Real-time fluorescence quantitative PCR

One-step ligation of the phosphine-thioester elucidates the landscape of S-nitrosation proteome in lipopolysaccharide-related inflammation

Hui Ye, [*, a]（叶辉） Langlang Lv, [#, a, c] Jianbing Wu, [#, a, b] Hongtao Wen, [#, a, c] Yihua Zhang, [a, b] Zhangjian Huang [*, a, b, d]

[a]*State Key Laboratory of Natural Medicines,*
[b]*Jiangsu Key Laboratory of Drug Discovery for Metabolic Diseases,*
[c]*Jiangsu Provincial Key Laboratory of Drug Metabolism and Pharmacokinetics, China Pharmaceutical University, Nanjing 211198, P. R. China*
[d]*School of Pharmacy, Xinjiang Key Laboratory of Biopharmaceuticals and Medical Devices, Key Laboratory of Active Components of Xinjiang Natural Medicine and Drug Release Technology, Engineering Research Center of Xinjiang and Central Asian Medicine Resources, Xinjiang Medical University, Urumqi 830054, P. R. China*

**Correspondence email: zhangjianhuang@cpu.edu.cn .*

Abstract

Protein S-nitrosation (SNO), a post-translational modification elicited by nitric oxide (NO) on cysteine residues, regulates a large range of physiological processes including macrophage polarization. However, SNO modifications on the proteome have often been identified by a biotin switch technology (BST). The BST method reduces S-nitrosothiols to thiols and then labels the resulting thiols. Alternatively, here we developed an SNO probe (SNOP) which can directly convert unstable SNO groups through a one-step ligation on the nitrosylated cysteine and enables straightforward identification of SNO modified sites with the aid of proteomics. We first demonstrated that the SNOP rapidly and selectively reacted with S-nitrosothiols. Thus, we used SNOP to enrich the SNO-modified proteins in CysNO-treated macrophages and identified 1838 SNO peptides, including 1146 SNO peptides heretofore unreported in the dbSNO database. To further examine the SNO-modified proteome in physiologically relevant conditions, we quantified the changes of SNO-modified proteins in M1-polarized macrophages using RAW264.7 cell lines and bone marrow-derived macrophages (BMDMs) following lipopolysaccharide (LPS) / interferon- γ (IFN γ) administration. Specifically, we identified 18 shared SNO sites (fold change $\geqslant$ 2, p value $\leqslant$ 0.05) in M1-polarized RAW264.7 and BMDM proteome. The 18 shared SNO sites are involved in cellular adhesion, glycolysis, and protein synthesis, potentially serving as key targets in regulating macrophage immune responses. Lastly, we measured SNO levels in various organs of mice after LPS injection via immunoblotting. Together, we showed that the SNOP with high reactivity and selectivity towards SNO modified peptides is a powerful tool for mapping SNO modified proteome and for elucidating NO-related pathophysiological changes and is compatible with both proteomic and immunoblotting analysis.

Key Words: S-nitrosation, nitric oxide, S-nitrosylation, proteomics, LPS, macrophage

Trityl-based biradical as EPR probe for superoxide radical with enhanced sensitivity

Yurui Leng（冷雨睿）, Yande Gao, Kailin Jiang, Guifang Han*, Yangping Liu*, Yuguang Song*

Tianjin Medical University, Tianjin, 300070

**Correspondence email: lengyurui0615@163.com*

Abstract

Triarylmethyl (trityl) radicals such as CT02-H and PST-NA are important spin probes for reliable measurement of superoxide radical ($O_2^{\bullet -}$) by electron paramagnetic resonance (EPR) spectroscopy owing to their high specificity to this reactive species. However, the measurement of $O_2^{\bullet -}$ is based on the EPR signal decay of these spin probes, which is unfavorable for the maximal detection sensitivity. In this work, we report the synthesis of a new trityl-based biradical dubbed as TOT for $O_2^{\bullet -}$. TOT exhibited a very weak and broad EPR signal under physiological conditions due to its strong spin-spin exchange interaction. Simulation of its solid-state EPR spectrum showed that TOT had a dipolar interaction of 24 G with the estimated spin-spin distance of 10.45 Å. The reaction of TOT with a low flux of $O_2^{\bullet -}$ led to the appearance of a new quartet signal due to the trityl monoradical which was generated by the $O_2^{\bullet -}$-induced spin quenching of one of the two trityl parts in TOT. As such, the growth of the intense EPR signal enabled highly sensitive measurement of $O_2^{\bullet -}$ with the detection limit of down to 8.7 nM/min over 60 min. Importantly, TOT exhibited high specificity against other biological oxidoreductants. Overall, our present study demonstrates that TOT has high specificity and sensitivity to $O_2^{\bullet -}$ and would find applications for measurement of a low flux of $O_2^{\bullet -}$, e.g. from the resting cells.

Browning effect of Inguinal White Adipose Tissue by a Novel Lignan (-)-Secoisolariciresinol 4-O-Methyl Ether, Modified from Arctigenin, Attenuates Diet-induced Obesity by Activating Mitochondria and Peroxisomes

Jiao Wenjun

Kyung hee university

**Correspondence email: jiaowenjun@naver.com*

Abstract

Studies indicate that the induction and activation of brown and beige adipocytes, which can enhance energy expenditure, may be beneficial for managing obesity and its associated diseases. This study investigated whether a novel lignan (-)-secoisolariciresinol 4-O-methyl ether (S4M) obtained from arctigenin inhibited diet-induced obesity by the browning of white adipose tissue (WAT). S4M treatment inhibited adipogenesis and lipid accumulation in white-induced 3T3-L1 adipocytes and in zebrafish embryonic development. Moreover, S4M treatment promoted browning in white adipocytes by increasing the protein levels of TOM20, UCP1, and PGC1 α and consequently upregulating mitochondrial content. S4M treatment significantly promoted mitochondrial fission by increasing the expression of DRP1. Furthermore, it enhanced peroxisome biogenesis and function by inducing PEX13, ACOX1, and catalase. Mdivi-1, a mitochondrial dynamics inhibitor, diminished the browning effect of white adipocytes by the S4M treatment. This study found that S4M treatment inhibited weight gain in HFD-induced obese mice, decreased the weight of WAT, and increased the abundance and function of mitochondria and peroxisomes in inguinal WAT, suggesting that S4M treatment could increase energy expenditure. The results show that S4M could potentially be used as a therapeutic agent to address obesity and its associated diseases.

Key Words: (-)-secoisolariciresinol 4-O-methyl ether, Anti-obeisty, Redox Biology, Reactive Oxygen Species

CPD84: A Novel PPI inhibitor Targeting ELF3-PtnA Interaction to Modulate Angiogenesis in Ovarian cancer

Inhye Moon,[1] Seung Hee Seo,[1] and Youngjoo Kwon[1,2]*

[1]*Graduate School of Pharmaceutical Sciences,* [2]*College of Pharmacy, Ewha Womans University, Seoul, 03760, Korea,*

**Correspondence email: ykwon@ewha.ac.kr*

Abstract

Ovarian cancer is the fourth-highest mortality cancer in women. In the case of high-grade ovarian cancer, the five-year survival rate is remarkably low because of its late diagnosis and high recurrence and metastasis rates. In general, angiogenesis is an important factor in promoting the growth and metastasis of ovarian cancer. Therefore, inhibiting angiogenesis is a common therapeutic strategy to suppress ovarian tumor progression.

Angiogenesis is significantly promoted under hypoxic condition, and such process is known to be regulated by various transcription factors such as HIF-1 α . In our previous study, it was verified that HIF-1 α transcriptionally regulate the expression of ELF3. In addition, the ovarian cancer database analysis found that ELF3 had a direct effect on ovarian cancer patients with high recurrence rates.

The transcriptional activity of ELF3 is determined by its interaction with co-activators. In this study, ELF3 was newly found to interact with a partner protein A (named PtnA, due to patent issues) as a co-activator and this protein-protein interaction (PPI) between ELF3 and PtnA played an important role in the upregulation of the various genes related to angiogenesis. Thus, we discovered PPI inhibitor CPD84 that potently inhibited the ELF3-PtnA interaction and confirmed this PPI inhibition could suppress the expression level of angiogenic factors. The antiangiogenic efficacy of CPD84 in vivo and in vitro was also validated.

Development of nitric oxide-donating Netarsudil derivatives as a synergistic therapy for glaucoma with reduced ocular irritation

Cunrui Li（李存睿）

State Key Laboratory of Natural Medicines, China Pharmaceutical University, Nanjing 211198, P. R. China.

**Correspondence email: cunruili@stu.cpu.edu.cn*

Abstract

Based on the synergistic therapeutic effect of nitric oxide (NO) and Rho-associated protein kinase (ROCK) inhibitors on glaucoma, a series of NO-donating Netarsudil derivatives were designed, synthesized, and their activities in vitro and in vivo were evaluated. Among them, (S)-10e released an appropriate amount of NO in aqueous humor in vitro and displayed potent ROCK inhibition. Topical administration of (S)-10e significantly lowered intraocular pressure in an acute ocular hypertension rabbit model and protected retinal ganglion cells in a magnetic microbead occlusion mouse model. A metabolism investigation revealed that (S)-10e released 7a, a metabolite after NO releasing, and 13, an active metabolite of (S)-Netarsudil, in rabbit eyes. Notably, introducing an NO donor moiety attenuated ROCK inhibition-induced ocular irritation in an sGC-independent manner, suggesting that the attenuated conjunctival hyperemia effect of (S)-10e is related to the NO-induced protein S-nitrosation of phosphodiesterase 3A (PDE3A). Overall, (S)-10e is a promising candidate for glaucoma treatment.

Development of novel trityl radicals as efficient buffers for superoxide radical via unprecedented reversible reactions

Longfei Gao（高龙飞）, Qi Shao, Meirong Feng, Yuguang Song* and Yangping Liu*

Tianjin Key Laboratory on Technologies Enabling Development of Clinical Therapeutics and Diagnostics, School of Pharmacy, Tianjin Medical University, Tianjin 300070.

**Correspondence email: gaolongfei0409@outlook.com*

Abstract

Superoxide radical ($O_2^{\bullet-}$) is one of reactive oxygen species that can undergo redox reactions, nucleophilic substitution reactions and addition reactions with diverse substrates. However, due to its high reactivity, the $O_2^{\bullet-}$-involved reactions are almost destructive, resulting in different oxidation products. In this study, we report an unprecedented reversible radical addition reaction between $O_2^{\bullet-}$ and benzyl ether-substituted trityl radicals (TBOR) which affords the corresponding superoxide adducts (TBOR-OOH). The formation of TBOR-OOH was confirmed by electron paramagnetic resonance (EPR) spectroscopy, LC-MS and UV-Vis spectroscopy. Interestingly, TBOR-OOH was unstable in phosphate buffer and converted back to TBOR gradually with the regeneration of $O_2^{\bullet-}$ as shown by EPR spin-trapping experiments. Moreover, we found that TBOR-OOH can be reduced in situ to the stable hydroxyl adduct (TBOR-OH) in the presence of reducing agents such as methyl sulfide and thiols. Interestingly, photoirradiation of TBOR-OH released the original trityl TBOR and generated hydroxyl radical (•OH) in a quantitative manner. Therefore, TBOR-OH can serve as a light-responsive and oxygen-independent •OH donor, which would find applications in photodynamic therapy. Overall, our work presents the first example for the reversible addition reaction of $O_2^{\bullet-}$ and TBOR could be used as an effective "$O_2^{\bullet-}$ buffer" to modulate the levels of $O_2^{\bullet-}$ in biological systems.

Discovery of Selective Cathepsin S Inhibitors as Potential Therapeutic Agents for Triple-Negative Breast Cancer

[1]Yi Liu, [2]Younghwa Na, [1]Youngjoo Kwon*

[1]College of Pharmacy, Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul, 03760, Korea,

[2]College of Pharmacy, CHA University, Pocheon, 11160, Korea.

**Correspondence email: ykwon@ewha.ac.kr.*

Abstract

Cathepsins are a group of proteases, with approximately 15 different classes in humans, that function primarily within the acidic environment of lysosomes. Among them, Cathepsin S (CTSS), a lysosomal cysteine protease belonging to the peptidase C1 family, plays a crucial role in the degradation of unwanted and damaged proteins, antigen processing, and the cleavage of substrates both intra- and extracellularly across a broad pH range.

Triple-negative breast cancer (TNBC) is characterized by the absence of estrogen and progesterone receptors and a lack of overexpression of the epidermal growth factor receptor 2 gene. TNBC is notably more aggressive than other breast cancer subtypes, with higher rates of recurrence and metastasis, leading to a poorer prognosis. Currently, chemotherapy is the only systemic treatment available for TNBC, yet only 30% of patients achieve a pathologic complete response. Elevated levels of CTSS in TNBC tissues have been linked to increased tumor invasion, and studies have shown that combining a CTSS inhibitor with chemotherapy enhances treatment efficacy. These findings suggest that targeting CTSS could be a promising therapeutic strategy for TNBC.

In this study, we conducted an in vitro assay to screen 151 newly synthesized compounds in search of a novel, selective CTSS inhibitor. Following the screening, four compounds exhibited significant CTSS inhibitory activity. We then performed selectivity tests to confirm that these compounds were more selective for CTSS over other cathepsins. Finally, we conducted docking studies to identify the binding residues of these compounds within the CTSS crystal structure.

Genome-wide CRISPR Screening of Genes Regulating Endoplasmic Reticulum H_2O_2

Zhu Qiaoli [1,2]（朱乔丽）, Chen Chang[1*]

1 Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China;

2 University of Chinese Academy of Sciences, Beijing, 100049, China

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Redox homeostasis is an equilibrium between reducing and oxidizing reactions within cells. However, the redox regulatory network is far from clear. Since the endoplasmic reticulum (ER) is a dynamic organelle orchestrating the folding and post-translational maturation of almost all membrane proteins and most secreted proteins, redox regulation of ER is delicate and sensitive to perturbation. In order to discover new genes participating in ER H_2O_2 regulation, we combined CRISPR/Cas9 gene editing technology with genetically encoded fluorescent probe named HyPerion, and constructed a HeLa cell line stably expressing Cas9 and ER-located-HyPerion. The cells were affected with viruses to knock out each gene, and the flow cytometry was used to sorted out cells with the intensity of top 5% and lowest 5%, which was expected to distinguish the most oxidative and the most reductive cells with specific gene knocked out. Two rounds of screening were carried out and the genomic DNA was extracted for next-generation sequencing. Analysis of the next-generation sequencing provided us with a table containing candidate genes to regulate ER H_2O_2. Among these candidates, a transmembrane gene located in the ER attracted our attention. The level of ER H_2O_2 was significantly upregulated when it was knocked down by siRNA. More interestingly, its knockdown by siRNA significantly upregulated the expression of ERO1 α. Further research is needed to study whether it induces H_2O_2 through up-regulation of ERO1 α and illustrate the specific molecular mechanism. Our discovery of the new gene regulating ER H_2O_2 would help extend the knowledge of the redox regulatory network, which is of great significance in the field of redox research.

Key Words: Endoplasmic reticulum (ER), redox, gene

GTSE1 promotes pulmonary fibrosis through the induction of EMT

Hee Jin[1], So-Yeon Park[1], Hangyeol Park[1], Michaela Jeong[1], Hyukjin Lee[1], Jaeho Cho[2], Yun-Sil Lee[1]

1.Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul 120-750, Korea

2.Department of Radiation Oncology, Yonsei University Health System, Seoul 120-749, Korea

**Correspondence email: hee_jin@ewha.ac.kr*

Abstract

G2 and S phase-expressed protein 1 (GTSE1) has emerged as a significant contributor to the development of pulmonary fibrosis (PF), particularly idiopathic pulmonary fibrosis (IPF). Through comprehensive genomic analysis of IPF patient samples, we observed a marked elevation of GTSE1 expression in fibrotic lung tissues, contrasting with minimal expression in normal lung tissues. Further bioinformatics analyses linked GTSE1 upregulation to an enhanced epithelial-to-mesenchymal transition (EMT) gene signature, prompting us to explore its interaction with EMT-related transcription factors. Mechanistically, we discovered that GTSE1 promotes EMT by stabilizing the zinc-finger E-box-binding homeobox 1 (ZEB1) protein, specifically by binding to the unphosphorylated form at Ser585, thereby preventing its degradation. This stabilization of ZEB1 correlates with increased collagen accumulation and greater fibrosis severity in both IPF patient tissues and PF mouse models. Notably, pulmonary delivery of nanoparticle-mediated RNA targeting GTSE1 effectively suppressed ZEB1 expression and mitigated disease progression in bleomycin- and radiation-induced PF mouse models. These findings identify the GTSE1–ZEB1 axis as a critical driver of pathological EMT in PF and highlight GTSE1-targeting strategies as a promising therapeutic approach for PF.

Key Words: GTSE1, ZEB1, Epithelial-mesenchymal transition, Pulmonary fibrosis

In Situ Generation and High Bioresistance of Trityl-based Semiquinone Methide Radicals under Anaerobic Conditions in Cellular Systems

Xizi Du（杜习姿）, Shuai Li, Yuguang Song* and Yangping Liu*

Tianjin Key Laboratory on Technologies Enabling Development of Clinical Therapeutics and Diagnostics, School of Pharmacy, Tianjin Medical University, Tianjin 300070

**Correspondence email: m17877780434@163.com*

Abstract

Tetrathiatriarylmethyl (trityl) radicals have found wide applications as spin probes/labels for electron paramagnetic resonance (EPR) spectroscopy and imaging due to their excellent EPR properties. Although trityl radicals have been long considered to be bioresistant and much more stable than nitroxide radicals, the significant decay of trityl-based spin label tagging to proteins was also observed in cells, thus limiting their in-cell applications. To address this issue, we herein report two trityl-based semiquinone methide radicals (OXQM• and CTQM•) which exhibit unprecedented high stability in cellular systems. Both radicals have relatively low pKa’s and exhibit EPR single line signals at physiological pH. Moreover, the in situ bioreduction of the quinone methide precursor OXQM in three cell lysates produced the radical form OXQM• in a quantitative manner which was most likely mediated by flavoenzymes. Importantly, the resulting OXQM• exhibited extremely high stability in the E.coli lysate under anaerobic conditions with 76- and 14.3-fold slower decay kinetics as compared to the trityl OX063 and a gem-diethyl pyrrolidine nitroxide. Intracellular delivery of OXQM into HeLa cells was also achieved by covalent conjugation with a cell-permeable peptide as evidenced by the stable intracellular EPR signal from the OXQM• moiety. Owing to the extremely high resistance of OXQM• towards bioreduction, OXQM and its derivatives would find wide applications in in-cell EPR and in-cell DNP studies for various cells which can endure short-term anoxic treatments.

MS-based Exclusive Isolation Study Unveils a Novel Anti-Melanogenic Phenolic Glycoside from Idesia Polycarpa Maxim

Bo-Yeong Yu, Jung-Eun Lee, Young-Sam Keum*

College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University, Goyang 10326, Korea.

**Correspondence email: bo073@naver.com*

Abstract

Various parts of Idesia polycarpa Maxim have been studied with their broad spectrum of biological activities. However, the bioactivities and chemical properties of the roots of I. polycarpa remain uninvestigated. This study aimed to elucidate bioactive compounds isolated from I. polycarpa Maxim and investigate the anti-melanogenic activity and the mechanism of the isolated compound in α-MSH-induced B16F10 melanoma cells. Among the isolated compounds, compound 1 reduced the melanin production in α-MSH-induced B16F10 cells along with the inhibition of tyrosinase (TYR) activity. In addition, compound 1 inhibited the expression of TYR, tyrosinase-related protein-1, and tyrosinase-related protein-2 by downregulating the expression of microphthalmia-associated transcription factor (MITF). Compound 1 inhibited MITF transcriptional activity by inhibiting the α-MSH/MC1R signal. In addition, compound 1 exerts an antioxidant effect by activating Nrf2 and detoxifying ROS. The antioxidant effect of compound 1 leads to inhibition of melanin production. The above results demonstrate that the MS/MS-based molecular networking analysis is a rational approach to discover bioactive compounds from the crude extracts of I. polycarpa, and compound 1 from I. polycarpa roots is expected to be an anti-melanogenic natural product.

Key Words: Microphthalmia-associated transcription factor (MITF), Tyrosinase (TYR), Melanin, Idesia polycarpa, Reactive Oxygen Species

Optimization for Bioactive Compounds, Antioxidant Activity of Complex Extract Containing Three Herbs Grown in Korea Using a Simplex-Centroid Mixture Design

Jeoung-Gyu Lee[1], Woo-Kyung Chung[1], Min-Jeong Ha[1], In-Hye Jo[1] and Ae-Son Om[1*]

[1] *Department of Food and Nutrition, College of Human Ecology, Hanyang University, Seoul 04763, Republic of Korea*

**Correspondence email: aesonom@hanyang.ac.kr*

Abstract

The aim of this study is to optimize the bioactive compound composition and antioxidant activity of a complex extract derived from three medicine herbs—Camellia sinensis, Cirsium japonicum, and Dendranthema zawadskii var. latilobum (Maxim.) Kita — cultivated in Korea. Using a simplex centroid mixture design, we systematically evaluated various antioxidant properties of the crude extracts and their combinations, including DPPH radical scavenging activity (DPPH), ABTS radical scavenging activity (ABTS), total phenolic content (TPC), and total flavonoid content (TFC). One-way ANOVA analysis indicated that the quadratic and special quadratic models were statistically significant for DPPH and ABTS assays, while the linear model was significant for TPC and TFC, as determined by ordinary least squares (OLS) regression. Pearson correlation analysis further revealed a strong positive correlation between TPC and TFC with both DPPH and ABTS ($p < 0.01$). From a set of 99 generated formulations, we identified an optimal mixture comprising 77.13% C. sinensis, 11.97% C. japonicum, and 10.90% D. zawadskii var. latilobum, with a desirability score of 1.0, which demonstrated high levels of the response variables. Experimental validation of this formulation showed that the observed values were within 1.5% of the predicted means, as derived from our polynomial regression models. These results were the promising antioxidant properties of the polyherbal mixture, supporting its potential as a potent antioxidant formulation.

Protective roles of supersulfides on acetaminophen induced liver injury

Chunyu Guo[1], Hiroyasu Tsutsuki[1], Katsuhiko Ono[1], Yukio Fujiwara[2], Stephen Lindahl[3], Ming Xian[3], Tomohiro Sawa[1*]

1.Department of Microbiology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto 860-8556, Japan
2.Department of Cell Pathology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto 860-8556, Japan
3.Department of Chemistry, Brown University, Providence, RI 02912, USA

**Correspondence email: sawat@kumamoto-u.ac.jp;chunyuguo1029@163.com*

Abstract

Acetaminophen (APAP) is a widely used antipyretic and analgesic drug in clinic, but excessive APAP can cause acute liver injury and even liver failure. The main pathogenesis of APAP induced liver injury is hepatocyte glutathione (GSH) depletion and inflammation. Supersulfides such as persulfide and polysulfide species have various biological effects including biosynthesis of sulfur-containing molecules, antioxidant stress and anti-inflammatory functions. We have developed supersulfide donors including N-acetyl-L-cysteine tetrasulfide (NAC-S2) and thioglucose tetrasulfide (TGS4) that effectively increase intracellular supersulfides (Cell Chem Biol 2019, Redox Biol 2024, Int Immunol 2024). More importantly, those chemical donors exhibit potent anti-inflammatory activities. Along this line, here we investigate the applicability of NAC-S2 on APAP-induced acute liver injury model. Severe liver injury and inflammation were triggered by APAP, whereas NAC-S2 treatment remarkably alleviated liver injury and suppressed the inflammation progression. Sulfur atom is the effector molecule of NAC-S2, which exerted the therapeutic effect mostly through suppressing the polarization of M1 macrophages as revealed by the decreased expressions of iNOS that were remarkably upregulated by APAP exposure. Moreover, NAC-S2 treatment not only increased the level of GSH and cysteine in liver tissue, but also increased the hydropersulfides/polysulfides of cysteine and GSH, which protected liver damage caused by GSH depletion. We thus anticipate the application of NAC-S2 as a therapeutic regimen for APAP induced liver injury as well as other inflammatory diseases and disorders.

Single-Cell Analysis Reveals Cell-Specific Patterns and Spatiotemporal Regulation of Nuclear Redox State

Miaoling Yang[1,2]（杨淼泠）

1.Institute of Genetics and Developmental Biology, Chinese Academy of Sciences

2.University of Chinese Academy of Sciences

**Correspondence email: yangmiaoling@genetics.ac.cn*

Abstract

The redox state, defined as the balance between oxidized and reduced molecular species, is a fundamental aspect of cellular metabolism, impacting energy production, signal transduction, and protein function. While extensive studies have explored redox regulation in cellular physiology, post-embryonic development, and aging, the dynamics and regulation of redox states during embryogenesis remain poorly understood. To address this gap, we performed single-cell, high-temporal-resolution stoichiometry of redox states in C. elegans early embryogenesis. Using genetically encoded biosensors and live imaging, we mapped glutathione redox potential in individual nuclei with a ubiquitously expressed Grx1-roGFP2 fluorescence biosensor. This approach enabled us to generate a comprehensive, minute-by-minute map of nuclear redox dynamics across every early cell. This atlas reveals highly spatiotemporally specific redox patterns, with distinct cell types displaying characteristic redox states that undergo temporal transitions to achieve their specific states. Notably, these cellular redox states can be accurately predicted by the combinatorial expression of oxidoreductase genes, which displayed strong developmental specificity in their expression and associated metabolic pathways. Additionally, our functional genomic analysis prioritized over 20 transcription factors that preferentially target oxidoreductase gene promoters or are functionally linked to these enzymes, laying a foundation for future mechanistic studies. Together, our work presents a cellular-resolution redox atlas of embryogenesis in a metazoan species and provides insights into the spatiotemporal dynamics and regulation of redox states.

Key Words: Nuclear Redox State, High-spatiotemporal resolution, Embryogenesis, Glutathione

Supersulfides protect against SARS-CoV-2 infection via suppression of the viral thiol proteases

Jia Yao[1], Tetsuro Matsunaga[1,2], Masanobu Morita[1], Seiryo Ogata[1], Minkyung Jung[1], Uladzimir Barayeu[1], Tsu yoshi Takata[1], Hozumi Motohashi[3], Takaaki Akaike[1]

[1]*Department of Environmental Medicine and Molecular Toxicology, Tohoku University Graduate School of Medicine*

[2]*Center for Integrated Control, Epidemiology and Molecular Pathophysiology of Infectious Diseases, Akita University*

[3]*Department of Medical Biochemistry, Tohoku University Graduate School of Medicine*

**Correspondence email: yaoj08166@gmail.com*

Abstract

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continually poses serious threats to global public health, and development of specific antiviral drugs against SARS-CoV-2 needs to be urgently developed. We found that supersulfides have strong nucleophilic and antioxidant activities and work defensively in bacterial infections and inflammatory pathologies. Supersulfides are also reported that they react with protein thiols in a manner that depends on the redox status of the thiol moieties. In this study, we examined the anti-SARS-CoV-2 effects of supersulfides by targeting viral thiol proteases.

SARS-CoV-2 has two different thiol proteases, papain-like protease (PLpro) and 3CL protease (3CLpro) that are essential for intracellular virus replication. We prepared recombinant proteins of the two thiol proteases and measured their protease activities after treatment with GSSSG or inorganic supersulfide donors such as Na2S2-4. These supersulfides showed strong the thiol protease inhibitory activity to both PLpro and 3CLpro. Furthermore, supersulfides were found to inhibit viral infectivity by cleaving disulfide bonds and causing conformational changes in spike proteins on the viral surface, as well as in thiol proteases. In fact, when supersulfides added to SARS-COV-2-infected VeroE6/TMPRSS2 cells which overexpress type II transmembrane serine protease, the viral replication in the infected cells was dramatically reduced. In addition, analysis using a Syrian hamster infection model showed that GSSSG treatment attenuated weight loss in infected hamsters and significantly reduced lesion area and viral load in infected lungs.

In this study, we revealed that supersulfides have antiviral effects that target the thiol proteases of SARS-CoV-2. In addition to the anti-viral activity, GSSSG is known to have a strong protective function that can modulate host immune reactions. Therefore, supersulfides has a great potential to be therapeutic agents for COVID-19 by acting on multiple points in infection mechanism of SARS-COV-2.

The function of sulfite oxidase in mitochondrial supersulfide metabolism

Yingchi Xia[1]（夏应驰）, Masanobu Morita[1], Seiryo Ogata[1], Tetsuro Matsunaga[1,2], Uladzimir Barayeu[1], Jung Minkyung [1], Naim Hassan[1], Tsuyoshi Takata[1], Hozumi Motohashi[3], Takaaki Akaike[1]

[1]*Department of Environmental Medicine and Molecular Toxicology, Tohoku University Graduate School of Medicine*

[2]*Center for Integrated Control, Epidemiology and Molecular Pathophysiology of Infectious Diseases, Akita University*

[3]*Department of Medical Biochemistry, Tohoku University Graduate School of Medicine*

**Correspondence email: yingchixia1@163.com*

Abstract

Background: Sulfite oxidase (Suox) deficiency, an inherited disorder, causes to severe neurological complications in newborns and frequently leads to early mortality. It is biochemically characterized by the accumulation of sulfite, thiosulfate, and S-sulfocysteine in tissues, as well as their elevated excretion in urine. Supersulfides that contained catenated sulfur moieties of each molecular structure serve as electron acceptors in mitochondrial respiration, indicative of their conservation across all organisms. The role of Suox in supersulfide metabolism is considered significant, however, it remains largely unknown. Here, we generated Suox knockout mice to investigate the role of Soux for supersulfide metabolism in mitochondria.

Methods and Results: Heterozygous Suox mice (Suox+/-) were generated with CRISPR-Cas9 system. The Suox+/- mice were intracrossed to obtain homozygous Suox (Suox KO) mice. Suox KO mice showed mendelian distribution at the birth, however, Suox KO mice died within 10 days after birth with growth arrest. Various tissues from Suox KO mice were investigated for pathological analysis and supersulfide metabolome analysis. For supersulfide metabolome analysis, the tissues were subjected to liquid chromatography-tandem mass spectrometry (LC-MS/MS). Suox KO mice showed abnormal morphologies in various tissues and displayed a markedly altered supersulfide metabolome compared to wild type, including significant elevations of sulfite and thiosulfate.

Conclusion: This study indicates that Suox plays crucial roles in supersulfide metabolism and tissue homeostasis. Furthermore, while genetic disorders of Suox are known, it is expected that the analysis of these Suox KO mice will further contribute to better understanding of supersulfide metabolism.

Key Words: supersulfides, sulfite oxidase, mitochondrial energy metabolism, mitochondrial，redox biology

TRPC3-Nox2 complex formation participates in the progression of striated muscle atrophy

Di Wu[1] Koichi Ayukawa[1] Yuri Kato[1] Xinya Mi[1] Kazuhiro Nishiyama[1] Akiyuki Nishimura[2] Motohiro Nishida[1,2]

1.Department of Physiology, Graduate School of Pharmaceutical Sciences, Kyushu University

2.Division of Cardiocirculatory Signaling, National Institute for Physiological Sciences and Exploratory Research Center on Life and Living Systems, National Institutes of Natural Sciences

**Correspondence email:*

Abstract

Striated muscles, including cardiac muscle and red skeletal muscle which abundantly express myoglobin, plays a crucial role not only in systemic motor function but also in the homeostasis of blood/lymphatic circulation and energy metabolism. The muscle atrophy that comes with age and disease will lead to reduced systemic function. We have previously shown that the onset and progression of myocardial atrophy induced by the anticancer drug doxorubicin is mediated through the functional interactions between transient receptor potential canonical (TRPC) 3 protein and NADPH oxidase 2 (Nox2), which is responsible for ROS production, on the cardiac myocyte membrane. We also identified ibudilast, a bronchodilator, can inhibit TRPC3-Nox2 complex formation and showed that ibudilast significantly reduced the systemic muscle weight loss induced by doxorubicin. In the present study, we investigated whether TRPC3-Nox2 complex formation is a therapeutic target for skeletal muscle atrophy in muscular dystrophy. In the skeletal muscle tissue of Duchenne muscular dystrophy (mdx) model mice TRPC3-Nox2 protein complex formation was markedly observed. Pharmacological inhibition of this complex formation by ibudilast a suppressing trend in muscle weight gain and muscle cross-sectional area reduction was observed, attenuated skeletal muscle atrophy and motor functional loss in mdx mice. Furthermore, administration of pyrazole-3 (Pyr3), a TRPC3-selective inhibitor, to mdx mice similarly reduced ROS production by inhibit TRPC3-Nox2 complex formation and attenuated muscle atrophy and muscle weakness. These results suggest that TRPC3-Nox2 complex formation may be a new therapeutic target for the prevention of myopathic muscle atrophy.

Key Words: TRPC3, Nox2, ROS, muscle atrophy

Blockade of the TP Receptor Ameliorates the Ischemic Renal Disorders in PGIS Deficient Mice

Jiahui Ge[1]（葛佳辉）, Jing Leng[1], Xijian Chen[1], Xinya Shi[1], Dong He[1], Gang Yu[1], Yineng Xu[1] and Bin Liu[1]*

[1]*Cardiovascular Research Center, Shantou University Medical College, Shantou, China*

**Correspondence email: bliu@stu.edu.cn*

Abstract

Background PGI_2 synthase (PGIS) catalyzes the conversion of prostaglandin (PG)H_2 to PGI_2 and is expressed in various tissues, especially in vascular endothelial and smooth muscle cells. Prostacyclin-deficient (*Pgis*$^{-/-}$) mice can develop hypertension, ischemic renal disorders, cardiac hypertrophy and so on. In our recent research, PGIS deficiency results in a switching of COX products from PGI_2 to $PGF_{2\alpha}$, PGE_2, and PGD_2, but not to TxA_2 in blood vessel, and leads to TP receptor activation.

Method Experiments were performed on WT, *Pgis*$^{-/-}$ and *Pgis*/thromboxane-prostanoid receptor gene (*Tp*) double knockout (*Pgis*$^{-/-}$*Tp*$^{-/-}$) mice. Concentrations of blood urea nitrogen（BUN）and creatinine（CRE）in serum were measurement by ELISA kit. Kidneys were embedded in paraffin, the sections (4 mm thickness) were stained by Masson's trichrome (MTC) staining. Parameters of fibrosis in kidney of mice were monitored at 24-26 weeks of age.

Result Additional ablation of TP receptor in *Pgis*$^{-/-}$ mice ameliorated the renal function, as evidenced by the levels of BUN and CRE. Meanwhile, fibrosis was observed in *Pgis*$^{-/-}$ kidney by using Masson's trichrome (MTC) staining and Western blotting. However, the functional and histological impairment were prominently alleviated in *Pgis*$^{-/-}$*Tp*$^{-/-}$ type.

Conclusion Our study demonstrates that the TP receptor plays an essential role in mediating the augmentation of the renal disorders when PGIS is deficient, suggesting TP as a promising therapeutic target in the kidney disorders associated with PGIS insufficiency.

Key Words: PGI_2 synthase (PGIS), TP receptor, renal disorder

Effect and mechanism of oligodendrocyte knockout of *Fpn1* in mice on depression-like behavior

Na Zhang*（张娜）

Hebei normal university, 050024, 20 South Second Ring Road East, Shijiazhuang province, China;

**Correspondence email: 823693865@qq.com*

Abstract

Iron is a trace element necessary to maintain the normal physiological functions of cells.In the nervous system, iron,as an important cofactor,is involved in a variety of important physiological processes,including myelination,neurotransmitter synthesis,synaptic development and energy production[17],and it plays a crucial role in the growth and conduction of the nervous system. Abnormal increase of iron in the brain will destroy the body's iron homeostasis.Lead to a variety of neuropsychiatric diseases,such as depression.The study found that in depressed patients/animal models,genetic changes associated with iron deposition were observed [27,30].The function of oligodendrocytes in the brain depends on the content of iron.The differentiation of oligodendrocytes is closely related to myelination, and the obstruction of myelination will lead to the change of synaptic outcome and affect the conduction of nerve impulses.However, the role of the change of iron in this process remains to be studied.In this study,the *Fpn1*-flox mouse and the Olig2-cre mouse were hybridized to obtain mouse with oligodendrocyte knockout of *Fpn1* gene. The WB,immunofluorescence staining,pathological staining,ELISA,cell culture and other methods were used to explore how the abnormal increase of iron affects the exercise of oligodendrocyte function.It can lead to depression.The results showed that the abnormal increase of iron in oligodendrocytes could lead to depression-like behavior,mainly due to the obstruction of myelin regeneration function and neurotransmitter synthesis and the change of synaptic structure,which eventually led to the obstruction of nerve conduction and ultimately resulted in depression-like behavior.Indicating that the change of iron metabolism could lead to depression-like behavior. Altering iron levels could be a new target for treating depression.

Key Words: Oligodendrocyte,*Fpn*1,Iron.

Hydrogen Sulfide Targets S-Sulfhydrated-cAMP-response element binding protein (CREB) Cys286 Residues to Inhibit the epithelial-mesenchymal transition (EMT) in Chronic Renal Injury

Shuai Chen[1,2]（陈帅）, Wen Wang[1,2]*

[1]*Department of Physiology and Pathophysiology, School of Basic Medical Sciences, Capital Medical University, No. 10 Xitoutiao, You An Men Wai, Beijing 100069, China.*
[2]*Beijing Key Laboratory for Metabolic Disorder-Related Cardiovascular Diseases, Beijing, China.*

**Correspondence email: wangwen@ccmu.edu.cn.*

Abstract

Background and Aims: The protective role of hydrogen sulfide (H_2S) has been shown in chronic kidney disease(CKD). cAMP-response element binding protein (CREB) is a crucial transcriptional factor involved in the development of fibrosis in multiple organs. However, its precise role in kidney disease and the related mechanism remain unclear.

Approach and Results: We showed that H_2S level was downregulated in hyperhomocysteinemia (HHcy) or cisplatin induced kidney dysfunction. Interestingly, the serum H_2S level was decreased and homocysteine level was increased on the first day after cisplatin injection, which were earlier than renal function indicators such as serum creatinine and urea nitrogen. Administration of NaHS (exogenous H_2S donor) alleviated kidney injury through epithelial-mesenchymal transition (EMT) pathway. Strikingly, S-sulfhydration of CREB was decreased in kidney injury models. The NaHS-mediated increase in CREB S-sulfhydration inhibited the nuclear translocation of itself and the consequent expression of inflammation and fibrosis factors. Cys286 residues of CREB was the effective S-sulfhydration site, which was located in nuclear localization sequence. To investigate the role of S-sulfhydrated CREB in renal injury, we constructed CREB Cys286 mutation plasmid and transfected into renal tubular cells. We showed that the protection conferred by H_2S was blocked by the mutation of CREB Cys286. Consistently, the transcriptional activity of CREB and EMT suppressed were reversed.

Conclusions: H_2S-mediated CREB S-sulfhydration alleviated kidney damage through EMT pathway. Hence, S-sulfhydrated-CREB may be an effective and potential therapeutic target for the treatment of CKD.

Key Words: H_2S, S-sulfhydration, CREB, EMT, CKD

Impact of tyrosine amination on the aggregation and neurotoxicity of amyloid-β : Unveiling a potential defensive mechanism in Alzheimer's disease

Ting Hu [1]（胡婷）, Zhonghong Gao [1,*], Hailing Li [1,*]

[1] *School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan, 430074*

**Correspondence email: zhgao144@hust.edu.cn; lihailing86@hust.edu.cn*

Abstract

Amyloid-β (Aβ) abnormal aggregation is closely associated with Alzheimer's disease (AD) development. Reactive nitrogen intermediates attack tyrosine residues in Aβ, forming 3-nitrotyrosine (3-NT). While tyrosine nitration is typically stable, recent research indicates that 3-NT can be reduced to 3-amino tyrosine (3-AT) *in vivo* [1]. Our study systematically investigated how tyrosine amination affects Aβ42's aggregation properties and neurotoxicity. Results demonstrate that tyrosine amination reduces the highly ordered β-structure content in Aβ42 aggregates, altering its multi-step secondary nucleation-dominated aggregation pathway. Consequently, fibrils fragment more easily, generating new growth ends, accelerating elongation rates, and promoting insoluble matter production. Despite nitration and amination of tyrosine inhibiting and promoting Aβ42 aggregation, respectively, both modifications decrease Aβ42's neurotoxicity by reducing intracellular ROS production and cell membrane damage. We further found that tyrosine amination alters the binding of Cu^{2+} with Aβ, resulting in the participation of Y10, which was originally not involved in coordination. In summary, tyrosine amino modification significantly alters Aβ42's aggregation properties, physiological characteristics, and metal ion coordination.

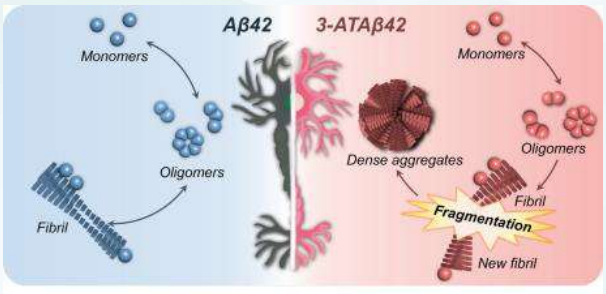


Fig. 1 The effect of tyrosine amination on amyloid-β (Aβ) aggregation and neurotoxicity. 3-ATAβ shares similar aggregation pathways with Aβ. However, 3-ATAβ exhibits an increased propensity for fibril fragmentation and deposition, thereby offering cellular protection against the toxicity of soluble oligomers.

Keywords： Amyloid-β; Alzheimer's disease; Oxidative stress; Tyrosine modification.

Reference

[1] Chen, L.; Yang, T.; Sun, X.; Wong, C.C.L.; Yang, D. *J. Am. Chem. Soc.* **2024**, **146**:11944-11954.

Insufficient S-sulfhydration of serum and glucocorticoid-regulated kinase 1 participates in hyperhomocysteinemia-induced liver injury

Xinyu Zhu（祝新宇）

Department of Pathology and Pathophysiology, School of Basic Medical Sciences, Capital Medical University

**Correspondence email:1450690431@qq.com*

Abstract

Background & Aims: Previous studies have established that hyperhomocysteinemia (HHcy) significantly contributes to the development of non-alcoholic steatohepatitis (NASH). Conversely, hydrogen sulfide (H_2S) has shown potential in mitigating NASH. Despite these findings, it remains uncertain whether H_2S can serve as a therapeutic agent against HHcy-induced liver damage.

Methods: We employed two experimental models:1. Animal Model: Mice were fed a high-methionine diet to induce HHcy. Cell Culture Model: HepG2 cells were exposed to homocysteine (Hcy). In both models, we assessed liver injury, H_2S concentration, and autophagy levels. Additionally, sodium hydrosulfide (NaHS), an H_2S donor, was used to test its potential in reversing hepatic pathological features induced by HHcy.

Results: 1) Hcy accumulation led to liver damage and increased autophagy. This was linked to insufficient S-sulfhydration of serum and glucocorticoid-regulated kinase 1 (SGK1) at Cys244 and Cys282, a crucial autophagy regulator. The deficiency in S-sulfhydration was resulted from downregulation of cystathionine-γ-lyase (CSE) and subsequent H_2S decrease, leading to SGK1 inactivation. 2) Administration of NaHS reduced the liver damage caused by high Hcy levels. NaHS supplementation restored H_2S levels, promoting the S-sulfhydration and activation of SGK1. 3) Pharmacological inhibition of SGK1 induced autosis, a specific type of cell death caused by overactivation of autophagy. Conversely, a constitutively active mutant of SGK1 ($SGK1^{S422D}$) significantly decreased autophagy and improved cell viability.

Conclusions: Our study concludes that NaHS supplementation mitigates HHcy-induced liver injury by downregulating hepatic autophagy through the S-sulfhydration and activation of SGK1. This post-translational modification by H_2S holds promise as a therapeutic approach for HHcy-induced liver damage. The potential therapeutic application of H_2S in treating liver injuries associated with HHcy presents a new avenue for research and clinical application.

Key Words: Hyperhomocysteinemia; Hydrogen sulfide; Serum and glucocorticoid-regulated kinase 1; S-sulfhydration; autophagy; liver injury

Near-infrared fluorescent probes for imaging vimentin in the brain of ischaemic stroke mice

Simiao Zhang[a]（张思淼）, Xin Wang,[a]* Ping Li,[a,c]* Bo Tang[a,b]*

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.* [b] *Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.* [c.] *College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic China*

**Correspondence email: lip@sdnu.edu.cn; xinwang@sdnu.edu.cn; tangb@sdnu.edu.cn*

Abstract

Ischemic stroke with high incidence and disability rate severely endangers human health. Current clinical treatment strategies are quite limited, new drugs for ischemic stroke are urgently needed. However, the existing methods of evaluating the efficacy of new drugs, such as the evaluation of neurological function, cerebral infarction size, and brain tissue water content, are mostly divorced from the real biological background, with single detection index and complex operation, resulting in large evaluation errors and delaying the process of drug development. Therefore, it is urgent to develop a method with real-time, in-situ, easy to operate, accurate and reliable pharmacodynamic evaluation. Vimentin is an important component of the cytoskeleton and is a crucial biomarker of cerebral ischemia and reperfusion. In this work, a responsive fluorescent probe Vim-NIG for near-infrared detection of vimentin in vivo was constructed for evaluating the efficacy of novel ischemic stroke drugs by taking advantage of fluorescence imaging's advantages of non-invasive, real-time, in-situ, high-selectivity, and high sensitivity. The probe, Vim-NIG, was modified according to the fluorescent dye new indocyocyanine green, and identified vimentin specifically by the homing peptide CHP targeting vimentin. When the probe was targeted to vimentin, it was accompanied by the assembled rotation of vimentin to restrict the rotation of benzindole, and emitted bright red fluorescence at 817 nm, which led to the specific recognition of vimentin. With the aid of this probe, we observed upregulation of vimentin in ischaemia-reperfused cells. Further, the same phenomenon was observed in ischemia-attention mouse brains. Meanwhile, vimentin showed a decreasing trend in the brains of ischemia-reperfused mice treated with edaravone dexborneol. This work achieves the detection of vimentin in ischemia-reperfusion cells and in vivo mice, and lays the foundation for further construction of a new platform for pharmacodynamic evaluation of ischemic stroke with higher accuracy.

Prostaglandin E_2 promotes platelet aggregation and thrombogenesis via Thromboxane A_2 receptor besides its canonic receptor EP3

Kaiqi Xie（谢恺麒）, Yukuan Chen（陈玉宽）, Jinwei Guo, Yingbi Zhou, Bin Liu*

Shantou University Medical College, 22 Xin-Ling Rd, Shantou 515041, China

**Correspondence email: 410398902 @qq.com*

Abstract

BACKGROUND: Prostaglandin E_2 (PGE_2) is a product of arachidonic acid metabolism and is critically involved in diseases with inflammation. This study aimed to determine how TP receptors act on platelet aggregation at lower concentrations of PGE_2, and whether TP receptors affect PGE_2 -mediated arterial thrombosis in vivo remain unclear.

METHODS: This study mainly used C57BL/6N and *Tp* $^{-/-}$, *Ep3* $^{-/-}$ and *Tp* $^{-/-}$*/Ep3* $^{-/-}$ mice of the same background, platelet aggregation experiment, high performance liquid mass spectrometry and mouse model of ferric chloride induced carotid artery thrombosis.

RESULTS: Our results suggest that low concentration of PGE_2 (≥ 0.01 μ M) could induce platelet aggregation through EP3 receptor and TP receptor without adding other platelet agonists in washed platelets; However, that's not the case in wild-type platelet-rich plasma. When we used ADP for preprocessing, PGE_2 acted on EP3 and TP can enhance platelet aggregation; Meanwhile, TXA_2 production was not observed in PGE_2 -induced platelet response detected by HPLC/MS to prove that this process is mediated by PGE_2. Compared with wild-type mice, less carotid thrombosis was induced in *Tp*$^{-/-}$ mice by ferric chloride; Next, we discovered that carotid artery thrombosis was observed in wild-type mice, but it was alleviated in *Tp*$^{-/-}$ mice after giving the same ozagrel treatment in the mouse model of carotid thrombosis induced by ferric chloride. In addition, TP receptor antagonists could inhibit the enhancement of human platelet aggregation induced by PGE_2, but that was no significant difference between the use of TP receptor antagonists alone and the use of TP receptor antagonists together with EP3 receptor antagonists.

CONCLUSIONS: PGE_2 can promote platelet aggregation at a low concentration (0.01-10μM) and involve in arterial thrombosis via Thromboxane A_2 receptor besides its canonic EP3 receptor.

Key Words: TP receptor, EP3 receptor, prostaglandin E_2 , platelet aggregation

Redox-inducible Radiomimetic Photosensitizers Selectively Suppress Cancer Cell Proliferation by Damaging DNA through Radical Cation Chemistry

Luo Wang（王洛）, Xuanwei Zeng and Huabing Sun*

Tianjin Medical University, Tianjin 300070

**Correspondence email: WL18361799458@163.com*

Abstract

Radiotherapy leverages ionizing radiation to kill cancer cells through direct and indirect effects, and direct effects are considered to play an equal or greater role. Several photosensitizers have been developed to mimic the direct effects of radiotherapy, generating radical cations in DNA models, but none has been applied in cellular studies. Here, we design a radiomimetic photosensitizer, producing DNA radical cations in cells for the first time. To reduce adverse effects, several redox-inducible precursors are prepared as cancer cells have elevated levels of GSH and H_2O_2. These precursors respond to GSH or H_2O_2, releasing the active photosensitizer that captures DNA abasic (AP) sites and generates DNA radical cations upon photolysis, without disrupting the redox state of cells. DNA radical cations migrate freely and are eventually trapped by H_2O and O_2 to yield DNA lesions, thus triggering DNA damage response. Our study suggests that direct effects of radiotherapy suppress cancer cell proliferation mainly by inducing G2/M phase cell cycle arrest, rather than promoting apoptosis. Synergistic effects of the precursor and chemotherapeutic agents are also observed in combination phototherapy. Beyond highlighting an alternative strategy for phototherapy, this proof-of-concept study affords a facile cellular platform to study the direct effects of radiotherapy.

Key Words: redox-dependent cytotoxicity, radiotherapy, DNA radical cations, phototherapy, 8-oxoguanine

S-nitrosation of CaMKIIα matters, a new mechanism mediating learning and memory

Boyu Chu[1,2]（褚博煜）, Xinhua Qiao[1], Chang Chen[1,2*]

[1] *Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China*
[2] *University of Chinese Academy of Sciences, Beijing 100049, China*

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Background: Ca^{2+}/calmodulin-dependent protein kinase II α (CaMKIIα) is closely related to learning and memory function. Our previous study found that CaMKIIα is *S*-nitrosated in mouse hippocampus and significantly decreased during natural aging. However, whether and how CaMKIIα *S*-nitrosation (SNO-CaMKIIα) mediates learning and memory remains unclear.

Results: Here, we surprisingly discovered that SNO-CaMKIIα physiologically increases during learning and memory tasks. To figure out whether SNO-CaMKIIα affects learning and memory, we construct the major CaMKIIα S-nitrosation sites mutant mice (C280/289V). C280/289V mice display learning and memory impairment in different forms of behavioral tests. And SNO-CaMKIIα mutation attenuates mice's long-term potentiation (LTP) and reduces the CaMKIIα kinase activity. The absence of CaMKIIα *S*-nitrosation alters synapsin I (SYNI) phosphorylation, which leads to increased presynaptic release probability. The abnormal increased presynaptic release causes AMPAR subunit unable to be further phosphorylated during learning and memory treatment, causing reductions in postsynaptic current response. The dynamic changes of AMPAR-mediated transmission, representing the changes of synaptic transmission, is reduced in C280/289V mice, which contributes to C280/289V mice's learning and memory impairments. Additionally, other model mice with learning and memory deficits, like Azheimer's disease model mice FAD^{4T} mice and nature aging mice, also display reduced dynamic changes of synaptic transmission.

Conclusion and significance: In summary, our findings demonstrated that SNO-CaMKIIα serves as a new mediator for learning and memory by regulating the dynamic changes of synaptic transmission. Our results provide valuable insights into *S*-nitrosation modification and learning and memory mechanisms and may offer potential intervention strategies for learning and memory impairment with precision redox regulation.

Key Words: Learning and memory, *S*-nitros(yl)ation modification, Ca^{2+}/calmodulin-dependent protein kinase II α, redox stress

The effect of water-soluble metalloporphyrin FeTPPS on membrane damage ar cytotoxicity induced by hIAPP

Zhilong Wang（王智龙）, Zhonghong Gao*, Hailing Li*

School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan, 430074, China

**Correspondence email: d202180146@hust.edu.cn*

Abstract

The deposition of Human islet amyloid polypeptide (hIAPP) aggregates is related to pancreatic β-cell dysfunction in Type 2 diabetes (T2D). A possible way of cytotoxicity induced by hIAPP may be through the disruption of cell membrane. In this study, we investigated the effect of water-soluble metalloporphyrin FeTPPS on membrane damage and cytotoxicity induced by hIAPP. We found that FeTPPS can inhibit amyloid formation of hIAPP in the presence of lipid membrane by ThT fluorescence assay, AFM and TEM. CD experiments indicated that the conformational transformation rate of hIAPP was slower in the presence of FeTPPS than that in the absence of FeTPPS. The dye leakage assay and hemolysis assay results showed that FeTPPS can inhibit the damage of model membrane and erythrocyte membrane induced by hIAPP, respectively. Moreover, we found that FeTPPS can reduce hIAPP induced cytotoxicity and damage to membrane of INS-1 cells. These results suggest that FeTPPS may have well potential for the treatment of T2D.

The *S*-nitrosation of CKMT1 exacerbates Parkinson's disease by restraining the intracellular energy shuttle

Tiepeng Wang [1]（王铁鹏）, Chang Chen[1*]

[1]*Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China*

**Correspondence email: changchen@moon.ibp.ac.cn*

Abstract

Nitrosative stress and energy depletion are pivotal contributors to the degeneration of neurons in multiple neurodegenerative diseases. CKMT1, crucial for maintaining cellular energy homeostasis, facilitates ATP/p-Creatine shuttling from mitochondria to the cytosol. We investigated the impacts and mechanisms of *S*-nitrosation on CKMT1 in MPTP-treated mice, an ideal Parkinson's disease (PD) model characterized by significant energy deficits in neuronal cells, as well as in *S*-nitrosoglutathione (GSNO)-treated neuro-2a cells. CKMT1 was validated to be *S*-nitrosatively modified at cysteine-63 both in the substantia nigra region of MPTP-injected mice and in neuro-2a cells. Functionally, *S*-nitrosation of CKMT1 resulted in delayed ATP recovery, reduced Cr/pCr flux efficiency, and diminished mitochondrial oxygen consumption rate (OCR) in cells, all of which were reversed by the C63A mutation. This mutation also enhanced the cell viability of neuro-2a cells and primarily cultured neurons under nitrosative stress. Mechanistically, *S*-nitrosation disrupted the oligomerization of CKMT1 from an octamer to dimers, thereby impairing ATP/p-Creatine shuttling. Molecular dynamics simulations revealed that *S*-nitrosation weakened salt bridges between adjacent CKMT1 dimers, destabilizing the octameric structure. The dissociation of octamer also diminished the interaction between CKMT1 and cardiolipin on the inner mitochondrial membrane and perturbed the functional association of the VDAC-CKMT1-ANT complex. $CKMT1^{C63A}$ mice were generated using CRISPR/Cas9-mediated knock-in technology. In the MPTP paradigm, mutant mice exhibited a notable reduction in CKMT1 *S*-nitrosation, an increased octamer/dimer ratio of CKMT1, elevated mitochondrial OCR and Cr/pCr flux efficiency, improved functional association of the VDAC-CKMT1-ANT complex, a significant increase in the number of dopaminergic neurons, and enhanced behavioral performance. Employing an LC-MS/MS-based method, we identified cysteine-63 as a conserved *S*-nitrosative modification site in mice with familial PD, mice with familial Alzheimer's disease (AD), and multiple brain tissues from aged mice, suggesting a universal regulatory role of this modification. In conclusion, *S*-nitrosation disrupted the oligomerization of CKMT1 and consequently restricted the functionality of the VDAC-CKMT1-ANT complex, inhibiting the transport of ATP from mitochondria to the cytoplasm. Elucidating the function and mechanism of this *S*-nitrosative modification provides novel clues for neuroprotective therapies.

Key Words: CKMT1, *S*-nitrosation, nitrosative stress, Parkinson's disease, energy shuttle

Screenings of nanoantibodies against protein disulfide isomerase and its antiplatelet aggregation effects

Wei Luo[1], Huiying Zhang[1], Mengchen Liu[1], Hongkuan Deng[2], Guozhen Cui[1,*]（崔国祯）

1. School of Bioengineering, Zhuhai Campus of Zunyi Medical University，Zhuhai, Guangdon, China

2. Department of Pharmaceutical Engineering, School of Life Sciences, Shandong University of Technology, Zibo, Shandong, China

**Correspondence email: cgzum@hotmail.com*

Abstract

Protein disulfide isomerase (PDI) is a multifunctional enzyme that catalyzes the oxidation, reduction, and isomerization of disulfide bonds, playing a critical role in the correct folding of nascent polypeptides within the endoplasmic reticulum. In addition to its intracellular functions, PDI is also known to modulate platelet activation and the coagulation system on the cell surface, positioning it as a key factor in thrombus formation. Here, we aimed to identify potent PDI inhibitors using single-domain antibodies (sdAbs), also known as nanobodies. These sdAbs are characterized by their small size (12–15 kDa), high antigen-binding affinity, low immunogenicity, and capability to target cryptic or concave epitopes. A human sdAb library with a diversity of 3×10^9 clones, derived from the VH framework (V3-23/D47), was used for three rounds of biopanning via phage display. This screening identified three sdAb sequences. Subsequent molecular docking studies conducted using MOE software, informed the selection of a promising candidate for recombinant expression. The purified sdAbs demonstrated potent inhibitory activity against PDI in an insulin turbidimetric assay. Furthermore, the sdAb effectively inhibited platelet aggregation in vitro when induced by arachidonic acid (AA), adenosine diphosphate (ADP), and platelet-activating factor (PAF). These new findings suggest a novel approach for the development of PDI-targeted antithrombotic therapies.

Key Words: protein disulfide isomerase; phage display; single domain antibody, antiplatelet

Analysis of the translation stalling sensor protein GCN1 complex using the proximity-dependent biotinylation enzyme TurboID.

Kazuki Hasegawa, Shuya Kasai, Yota Tatara, Junsei Mimura and Ken Itoh

Department of Stress Response Science, Biomedical Research Center, Hirosaki Graduate School of Medicine

**Correspondence email:*

Abstract

It has been revealed that the ribosome-binding protein GCN1, which is widely conserved in eukaryotes, recognizes and binds to ribosome collisions formed by translation stress, such as amino acid starvation or UV exposure, and is involved in translation-associated quality control by inducing mRNA decay and inhibition of translation initiation via eIF2a phosphorylation. Our previous analysis of Gcn1 knockout (KO) mice demonstrated that GCN1 is an essential gene for fetal growth and cell proliferation, and that tamoxifen-induced conditional KO (CKO) mice exhibit abnormal lipid metabolism in the liver. To elucidate the downstream pathways of GCN1 in vivo, we created a GCN1 fused with the proximity-dependent-biotinylation enzyme TurboID and a self-labeling protein HaloTag at the N-terminus of GCN1. We evaluated the amino acid starvation stress response in GCN1-deficient cells and confirmed that GCN1's function was maintained even after fusion with TurboID and HaloTag. In HEK293T cells, we expressed TurboID-HaloTag-GCN1 and comprehensively analyzed biotinylated proteins via mass spectrometry following biotin treatment. As a result, we identified the biotinylation of several ribosome-associated proteins, translation initiation factors, and cell cycle regulatory proteins. These findings suggest that these proteins form complexes with GCN1 and may act as regulators in response to translation stress.

Carbon dots cause developmental toxicity in zebrafish embryos via endoplasmic reticulum stress-mediated lipid dysregulation

Liwen Zeng（曾丽雯）, Xiaoyao Song

Department of Toxicology, School of Public Health, Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, MOE Key Laboratory of Geriatric Diseases and Immunology, Suzhou Medical College of Soochow University, Suzhou, Jiangsu 215123, P.R. China.

**Correspondence email: xysong@suda.edu.cn*

Abstract

Carbon dots (CDs) have been widely used due to their excellent physical and chemical properties, but their potential toxicities to human health have rarely been investigated, especially developmental toxicities. Herein, 2.5 nm CDs were synthesised by an electrochemical stripping method and used to study their developmental toxicity. Exposure to CDs resulted in increased mortality and malformation rates in zebrafish embryos, indicating their developmental toxicity. Further bioinformatics analysis suggested that CDs-induced lipid metabolism disorders may be an important mechanism of developmental toxicity in zebrafish embryos. Induction of endoplasmic reticulum stress (ERS) caused abnormal expression of lipid metabolism-related genes, leading to lipid accumulation in zebrafish embryos. Our results indicate that exposure to CD may lead to developmental toxicity through ERS-mediated lipid metabolism disorders, suggesting that CD may pose a threat to human health and must be considered when CD is incorporated into the environment and human life.

Key Words: Carbon dots, Endoplasmic reticulum stress, Transcriptomics, Lipid metabolism disorders

Ceruloplasmin deficiency in Leydig cells causes testicular dysfunction via iron-mediated oxidative stress in mice

Lihui Wu[1]（吴丽辉）, Shaomeng Kang[1]（康韶萌）, Yanzhong Chang[1*]

[1]*College of Life Sciences, Hebei Normal University, Shijiazhuang 050024, Hebei Province, China*

**Correspondence email: chang7676@163.com*

Abstract

The male factor accounts for more than 50% of infertility in approximately 15% of couples of childbearing ages worldwide. In the male reproductive system, testis is the most important organ which consists of germ cells and somatic cells. Leydig cells included in somatic cells can synthesize and secrete androgens such as testosterone, and play an important role in spermatogenesis and development. Iron participates in the normal physiological activities of the male reproductive system as an important cofactor in spermatogenesis and testosterone synthesis. However, iron overload can cause oxidative stress and ultimately can lead to male infertility. Therefore, the maintenance of iron homeostasis is important in the testis. Ceruloplasmin, as a ferroxidase, participates in the regulation of intracellular iron homeostasis. It also plays an antioxidant role in regulating the REDOX level of the body. In testis, Leydig cells, as the main storage site of ferritin, maybe play an important role in testicular iron metabolism. However, the role of ceruloplasmin in the testis remains unclear. Herein, we used *Cyp17a1*-cre transgenic mice to conditionally delete *Ceruloplasmin* (*Cp*) in Leydig cells. The data demonstrated that $Cp^{Cyp17a1}$-cKO mice had decreased sperm count and motility, organ coefficient of testis, and serum testosterone content. $Cp^{Cyp17a1}$-cKO mice showed elevated level of iron and ROS, decreased SOD level and inhibited cell proliferation in the testis, and possibly triggering ferroptosis through the HIF 1α/HO-1 pathway. In conclusion, our findings explore the effect of ceruloplasmin on male reproductive function and provided an important experimental basis for the clinical treatment of male infertility.

Domperidone induces apoptosis via inactivation of β-arrestin2-dependent MEK/ERK/STAT3 pathway in of human colon cancer cells

So Jin Sim and Kyung-Soo Chun*

College of Pharmacy, Keimyung University, Republic of Korea

**Correspondence email: chunks@kmu.ac.kr*

Abstract

Recently, the dopamine receptor D2 (DRD2), a G protein-coupled receptor, has been reported to play multiple roles in growth of tumor cells. The DRD2 carries out these functions by signaling through two transduces: G protein (Gαi) and β-arrestins. Domperidone is the DRD2 antagonist and prescribed for acute vomiting and gastroparesis. In the present study, we investigated whether domperidone induced apoptosis through the regulation of DRD2 activation in colon cancer HCT116 cells.

Treatment of HCT116 cells with domperidone induced apoptosis, which was associated with the cleavage of caspase-9, -7, -3 and PARP as well as the release of cytochrome C from mitochondria to cytosol. Domperidone treatment decreased in formation of β-arrestin2/MEK complex, which contributing to inhibition of MEK/ERK activation. Treatment with domperidone also diminished STAT3 activation and expression of cyclin D1, D2, D3 and survivin. Treatment of U0126, the MEK inhibitor, blocked phosphorylation of both ERK and STAT3. This result suggests the crosstalk between MEK/ERK and STAT3 signaling in domperidone-treated cells. In addition, the generation of ROS was increased during domperidone-induced apoptosis and the pretreatment of ROS scavenger Nacetylcysteine attenuated HCT116 cells from domperidone-induced cell death. Furthermore, domperidone significantly suppressed colon cancer cell xenograft tumor growth in nude mice.Our results provide evidence that the DRD2 antagonist domperidone induces apoptosis of HCT116 cells through inactivation of β-arrestin2-dependent MEK/ERK/STAT3 signaling pathway.

<Sim SJ.et al. Biomol. Ther.. 2024; Published online.>

Key Words: DRD2, colon cancer, apoptosis, STAT3, Reactive Oxygen Species

Environmental toxin exposure-induced oxidative stress impairs chromosome cohesion and segregation in mammalian oocytes

Yan Yun[1,2]（云彦）, Zhixiang Zheng[1], Neil Hunter[2]

1. Shantou Central Hospital, Shantou, China

2. Howard Hughes Medical Institute, University of California Davis, Davis, USA

**Correspondence email: yunyan365@163.com*

Abstract

A healthy oocyte is essential for a successful pregnancy and live birth, while oocyte development in mammals is susceptible to either physiological or environmental exposures. It has been well established that maternal aging, high fat diet induced-obesity, and environmental toxin exposure could induce elevated chromosome errors in mammalian oocytes, and these errors are the leading causes of early miscarriage, infertility and congenital disorders in humans.However, the underlying mechanisms are to be explored. Together with others, our previous work demonstrated that cohesion depletion is the leading factor causing chromosome segregation errors in mammalian oocytes. Interestingly, in diverse mouse oocyte models where chromosome errors are significantly increased, a negative association between oxidative stress and chromosome cohesion level was consistently established. For instance, the widespread herbicide atrazine exposure induced significantly reduced levels of cohesion and increased rates of chromosome abnormalities in mouse oocytes, and our further analysis indicated a positive correlation between atrazine exposure and levels of oxidative stress in oocytes. These data are consistent to a recent report showing elevated oxidative damage in Drosophila oocytes

caused weakening of chromosome cohesion and elevated chromosome errors. Therefore, we propose that oxidative damage might be the common risking factor causing cohesion deterioration and chromosome abnormalities in mammalian oocytes.

Karyoptosis is a cyclic AMP-responsive element binding protein 3 driven novel regulated cell death

Weidong Chen[1] and Yong-Yeon Cho[1*]

[1]*College of Pharmacy, The Catholic University of Korea, 43, Bucheon-si, Gyeonggi-do 14662, Republic of Korea*

**Correspondence email: cweidong06@gmail.com*

Abstract

Cyclic AMP-responsive element binding protein 3 (CREB3), a type II integral membrane protein, is recognized as a transcription factor activated through S1P/S2P-mediated cleavage, resulting in the formation of CREB3-CF via endoplasmic reticulum/Golgi complex vesicle trafficking. However, the molecular mechanisms underlying CREB3 activation as a transcription factor have been scarcely studied. In this study, we propose a novel hypothesis suggesting that the canonical pathway for CREB3 activation is replaced by the direct localization of full-length CREB3 (CREB3-FL) to the inner nuclear membrane (INM). In the INM, CREB3-FL interacts with nuclear lamina proteins, such as Lamin A/C and B, and chromatin DNA. Notably, mimicking the de-anchoring of CREB3-FL by overexpressing CREB3-FL-dTM (a transmembrane domain-deleted form) or CREB3-CF leads to a loss of nuclear membrane integrity. This results in increased nuclear lobulation and fragmentation, nuclear envelope rupture, loss of nuclear membrane integrity, and leakage of nuclear DNA into the cytoplasm. Since this ultimately results in cell death, we have designated this CREB3-mediated cell death phenomenon as "karyoptosis." Importantly, we have discovered that karyoptotic cell death is distinct from apoptosis, necroptosis, autophagy, and pyroptosis. Karyoptosis represents a novel form of regulated cell death with significant potential for application in next-generation human cancer therapies.

Key Words: CREB3, nuclear fragility, nuclear membrane, Karyoptosis, regulated cell death

Loss of poly(ADP-ribose) polymerase 1 boosts catalase activation via endothelin receptors

Jia-Bin Yu[1], Daeun Moon[2], and Jinu Kim[1,2,*]

[1] *Interdisciplinary Graduate Program in Advanced Convergence Technology & Science, Jeju National University, Jeju, Jeju Self-Governing Province 63243, Republic of Korea*

[2] *Department of Anatomy, Jeju National University College of Medicine, Jeju, Jeju Self-Governing Province 63243, Republic of Korea*

**Correspondence email: jaibinyu46@gmail.com*

Abstract

Nephrotoxins have been identified as agents that can lead to acute kidney injury (AKI) with significant risks of morbidity and mortality. Poly(ADP-ribose) polymerase 1 (PARP1) plays a critical role in the cellular response to DNA repair, resulting in cellular ATP depletion and subsequently necrosis when excessively activated. This research seeks to explore the involvement of PARP1 in AKI induced by aristolochic acid through the use of *Parp1* gene-absent mice. The absence of *Parp1* significantly mitigated renal dysfunction and tubular injury caused by aristolochic acid exposure, as evidenced by reduced levels of plasma creatinine and blood urea nitrogen, as well as lower tubular injury scores spanning from the cortex to the inner medulla. Aristolochic acid triggered excessive poly ADP-ribosylation, with a small portion attributable to PARP1 activation in the kidneys, as indicated by a slight decrease in poly ADP-ribosylation in aristolochic acid-exposed *Parp1*-absent kidneys. *Parp1* absence resulted in hyperactivation of catalase and an upregulation of endothelin 1 in the kidneys. However, the inhibition of PARP1 activation did not affect catalase activation and ET1 expression in proximal tubular cells, suggesting that the absence of PARP1-dependent poly ADP-ribosylation is not linked to them. The administration of a catalase inhibitor substantially worsened aristolochic acid-induced kidney dysfunction and tubular injury in *Parp1*-absent mice. Additionally, blocking endothelin receptors eliminated the protective impact of *Parp1* absence against AKI, along with catalase hyperactivation. These results indicate that the absence of PARP1 offers protection against aristolochic acid-induced kidney injury via catalase hyperactivation induced by the upregulation of ET1.

Key Words: acute kidney injury; aristolochic acid; poly(ADP-ribose) polymerase 1; catalase

Myriocin regulates cellular redox homeostasis via mitochondrial hormesis

Wenling Gu（顾文凌）, Weiyan Wang, Ke Liu*

Key Laboratory of Bio-Resources and Eco-Environment of Ministry of Education, College of Life Science, Sichuan University, 610065, Chengdu China

**Correspondence email: kliu@scu.edu.cn*

Abstract

Redox reactions play a vital role in the metabolic processes of the organism. The sphingolipid synthesis inhibitor Myriocin(Myr) possesses outstanding therapeutic potential in countering cellular oxidation and aging, and treating various metabolic diseases and major degenerative disorders in humans. Current research has initially disclosed the redox-related signaling pathways regulated by Myr. however, the molecular mechanism through which Myr governs these pathways remains elusive.

We initially detected the effect of Myr on the levels of mitochondrial reactive oxygen species (ROS) in the three cell lines of HeLa, STHdh, and SH-SY5Y. Subsequently, mitochondrial ROS was inhibited, and then the influence of Myr on the expression of PGC-1α , a key protein regulating mitochondrial function and cellular redox balance, was examined to verify the role of mitochondrial ROS. Since de novo sphingolipid synthesis takes place in the endoplasmic reticulum and is profoundly affected by Myr. The membrane interaction is the main Ca2+ transport route. Ca2+ in the mitochondrial matrix enhances electron transfer and ROS generation. we observed the endoplasmic reticulum-mitochondria coupling structure by electron microscopy and determined the effect on mitochondrial calcium ion level.

Myr induces alterations in the lipid composition of the endoplasmic reticulum membrane, promotes calcium ion transport that occurs in the endoplasmic reticulum-mitochondria coupling structure Mitochondria-associated ER membranes(MAMs), thereby elevating the calcium ion concentration in the mitochondrial matrix and increasing the generation of ROS. Low-dose ROS stimulation can trigger mitochondrial hormesis and thereby enhance the antioxidant capacity of cells. The mechanism by which Myr enhances the antioxidant capacity of cells and the feasibility of its application in the treatment of human diseases have been clarified.

Key Words: Myriocin，PGC-1α, ROS，mitochondrial hormesis，cellular redox

Protective Effects of OM2 Plant Extract against Oxidative Stress and Inflammation in Arsenic Exposed RAW264.7 cells

Hyejin Kim[1#], Woo-Kyung Chung[1#], Yujung Kim[1], Jeoung-Gyu Lee[1] and Ae-Son Om[1*]

[1] *Department of Food and Nutrition, College of Human Ecology, Hanyang University, Seoul 04763, Republic of Korea*

 # Contributed equally

**Correspondence email: aesonom@hanyang.ac.kr*

Abstract

Arsenic-induced oxidative stress and inflammation are significant contributors to various pathological conditions. This study investigated the protective effects of OM2 plant extract (OPE) against sodium meta arsenite (SA)-induced oxidative stress and inflammation in RAW264.7 cells. We evaluated the total phenolic content (TPC), total flavonoid content (TFC), and antioxidant activities (ABTS, DPPH, and FRAP assays) of OPE. The TPC and TFC of OPE were 321.78±2.27 mg GAE/g and 63.24±2.04 mg QE/g, respectively. The antioxidant activities at 500 μg/ml OPE showed significant radical scavenging and reducing power, with ABTS at 92.53±0.09%, DPPH at 66.80±0.94%, and FRAP value at 1272.25±14.02 μM $FeSO_4$.

OPE at concentrations of 10-200 μg/ml did not exhibit cytotoxicity by MTT assay. Notably, cell viability increased by 7.69%, 6.19%, and 7.89% at 10, 25, and 50 μg/ml OPE, respectively, compared to the SA-treated group. Further analysis using qRT-PCR and Western blot revealed a dose-dependent upregulation of HO-1, Nrf2, and PGC-1α mRNA, as well as HO-1 protein. The anti-inflammatory properties of OPE were confirmed by its ability to significantly reduce COX-2 mRNA and protein, as well as IL-1β, IL-6, and iNOS mRNA, when co-treated with LPS.

These results suggest that OPE exerts potent antioxidant and anti-inflammatory effects through the activation of HO-1, Nrf2, and PGC-1α, and the suppression of pro-inflammatory mediators. This study highlights the potential of OPE as a natural antioxidant and anti-inflammatory agent, with implications for its application in functional foods and therapeutic interventions. Further research is needed to explore the underlying mechanisms and potential clinical applications.

The effects of local iron treatment on intervertebral disc degeneration

Chenchen Li（李晨晨）, Yanzhong Chang

College of Life Sciences, Hebei Normal University, Shijiazhuang 050024, Hebei Province, China

**Correspondence email: lcc1195950399@163.com*

Abstract

Iron is the largest trace element in the human body, and it participates in a wide range of physiological functions and biochemical reactions. However, excessive iron can lead to the production of a large number of reactive oxygen species (ROS) by participating in electron transfer of the mitochondrial respiratory chain, which can lead to the destruction of mitochondrial structure and the disruption of mitochondrial function, as well as the induction of oxidative stress, lipid peroxidation and DNA damage. These events eventually lead to iron dependent programmed ferroptosis. ROS have been reported to be involved in apoptosis, autophagy, and senescence of nucleus pulposus cells, thereby altering the cellular phenotype and promoting disc degeneration. Recent studies have shown that ferroptosis caused by lipid peroxidation is also involved in disc degeneration. In the present study, the effects of local iron treatment on disc degeneration were explored using rat models. MRI (Magnetic Resonance Imaging) results suggested that local iron overload aggravated the degree of disc degeneration induced by acupuncture. Immunofluorescence staining showed that the degree of disc degeneration induced by acupuncture was associated with elevated iron levels in the tissue. After the administration of FAC liposomes, immunofluorescence staining showed that the expression of FTL, FTH, and MMP3 in the nucleus pulposus was further increased, while the expression of aggrecan was further decreased, suggesting that local iron overload aggravated the degeneration of the intervertebral disc. It was found that topical iron administration aggravated disc degeneration, and iron overload may promote disc degeneration by increasing oxidative stress.

The Function of 2-Mercaptoethanol in the Repair of DNA during Kidney Ischemia and Reperfusion through GPX4 Upregulation

Moon Daeun[1], Jia-Bin Yu[2], and Jinu Kim[1,2,*]

1Department of Anatomy, Jeju National University College of Medicine, Republic of Korea

2 Interdisciplinary Graduate Program in Advanced Convergence Technology & Science, Jeju National University, Republic of Korea

**Correspondence email: jinu.kim@jejunu.ac.kr*

Abstract

Kidney ischemia and reperfusion injury (IRI) is a significant contributor to acute kidney injury (AKI), which leads to elevated mortality rates. This condition results in DNA damage, which can occur due to various factors such as irradiation, oxidative stress, and IRI. 2-Mercaptoethanol (2-ME) serves as an antioxidant by scavenging hydroxyl radicals and offers defense against DNA damage in cells. The objective of this study was to investigate whether the administration of 2-ME could mitigate DNA double-strand breaks, consequently reducing kidney dysfunction and structural damage in tubules after IRI. The study involved inducing kidney IRI or conducting sham-operation on mice. The mice were then treated with 2-ME and/or Ras-selective lethal 3 (RSL3, a potent inhibitor of glutathione peroxidase 4 (GPX4)). Various aspects such as kidney function, tubular injury, DNA damage, expression of antioxidant enzymes, and activation of DNA damage response (DDR) kinases were evaluated. The results indicated that treatment with 2-ME notably alleviated kidney dysfunction, tubular injury, and DNA double-strand breaks following IRI. Among the DDR kinases, IRI stimulated the phosphorylation of ataxia telangiectasia mutated (ATM) and ataxia telangiectasia and Rad3 related (ATR), while reducing the phosphorylation of other DDR kinases including checkpoint kinase 1 (Chk1), Chk2, and X-ray repair cross complementing 1 (XRCC1). Treatment with 2-ME increased the phosphorylation of ATM and ATM-mediated effector kinases in kidneys subjected to IRI, indicating that 2-ME activates the ATM-mediated DDR signaling pathway. Additionally, 2-ME significantly upregulated GPX4 in IRI-subjected kidneys. Inhibition of GPX4 intensified the negative consequences of IRI, such as kidney dysfunction, tubular injury, DNA double-strand breaks, and inactivation of the ATM-mediated DDR signaling pathway in 2-ME-treated kidneys. These findings suggest that administration of 2-ME offers protection against DNA double-strand breaks post kidney IRI through GPX4 upregulation and ATM activation.

Key Words: 2-Mercaptoethanol, Ischemia and reperfusion injury, H2A.X variant histone, Glutathione peroxidase 4, DNA damage response, Ataxia telangiectasia mutated

The Role and Mechanisms of Prostaglandin E_2 Receptor EP3 in Acute Lung Injury

Zhengpeng Zeng[1,2]（曾征鹏）, Cheng Peng[1,2], Gang Yu[1,2], Yingbi Zhou[1], Bin Liu*[1,2]

[1]*Cardiovascular Research Center, Shantou University Medical College, Shantou, China*
[2]*Guangdong Provincial Key Laboratory of Infectious Diseases and Molecular Immunopathology, Shantou University Medical College, Shantou, China*

**Correspondence email: 974115114@qq.com*

Abstract

Background: Acute respiratory distress syndrome is a clinical challenge characterized by high incidence and mortality rates, with approximately 200,000 people affected worldwide each year and a mortality rate as high as 43%. In the process of inflammatory storm formation in inflammatory diseases such as acute lung injury, PANoptosis—pyroptosis, apoptosis, and necrosis—plays a key role in amplifying inflammation. In the state of pulmonary inflammatory diseases, the production of PGE_2 catalyzed by COX increases exponentially, exhibiting anti-inflammatory effects. However, the specific mechanisms remain unclear.

Methods: Wild-type (WT), Prostaglandin receptor Ep3 knockout ($Ep3^{-/-}$), and myeloid conditional Ep3 gene knockout ($Ep3^{F/F}Lyz2^{Cre}$) mice were utilized in our study. Prostaglandin expression levels in mouse lung tissues were detected using mass spectrometry. HE staining was employed to observe lung injury. Western blotting was used to detect the expression levels of relevant proteins and inflammatory factors in lung tissues. ELISA was conducted to measure inflammatory factors and DAMPS levels in bronchoalveolar lavage fluid and serum.

Results: Our findings showed that conditional knockout of Ep3 in myeloid immune cells ($Ep3^{F/F}Lyz2^{Cre}$) significantly alleviate lung injury in mice, and the expression of the upstream sensor protein Z-DNA binding protein 1 (ZBP1) involved in PANoptosis was notably reduced. Therefore, we hypothesized that this protective mechanism may primarily result from the inhibition of ZBP1-dependent PANoptosis mediated by conditional knockout of Ep3 in myeloid immune cells. Additionally, we observed that in the LPS-induced $Ep3^{-/-}$ mouse model of acute lung injury, blood pressure significantly decreased, and lung injury markedly worsened. We further hypothesized that in acute lung injury, parenchymal cell Ep3 may alleviate LPS-induced septic shock and play a crucial role in maintaining blood pressure stability.

Conclusions: The results of this study will reveal that conditional knockout of myeloid immune cell Ep3 can improve acute lung injury, while $EP3^{-/-}$ exacerbates septic shock and the specific regulatory mechanisms of acute lung injury.

Key Words: Acute lung injury, PANoptosis, Prostaglandin E_2, Prostaglandin receptor Ep3

Water-soluble single molecular probe for simultaneous detection of viscosity and hydrazine

Jiazi Yin [a] （尹佳子）,Yu Jin [b],Minhui Cao [a,*]Chao Yuan [a,b,*],Suhua Wang [b,*]

[a] *Guangdong Provincial Key Laboratory of Petrochemical Pollution Processes and Control, School of Environmental Science and Engineering, Guangdong University of Petrochemical Technology, Maoming 525000, China*
[b] *College of Science, College of Life Science and Technology, Huazhong Agricultural University, Wuhan 430070, China*

**Correspondence email: 18669912910@163.com*

Abstract

Hydrazine (N_2H_4) can cause serious damage to human health,while intracellular viscosity is highly associated with many diseases and cellular dysfunctions. Among other developed approaches in the past decades, organic small molecule probebased fluorescence methods are widely recognized as a powerful alternative featured with high sensitivity, simplicity, and visualization. However,to the best of our knowledge, N_2H_4 detection always involves the use of organic co-solvent in most of the probes developed, seriously hampering their biological applications.

Inspired by the works in which improved water solubility and biocompatibility could be achieved by the introduction of water-soluble monomers mainly represented by poly (ethylene glycol) for active molecules design, a novel probe with good water solubility and selectivity has been reported recently for N_2H_4 detection in colorimetric and ratiometric dual-manners, demonstrating the potential of organic molecules-based probe in biological application. Although most of those probes demonstrated fluorescence “turn on” response to both targets in different fluorescence channels, they still suffered from poor water solubility.

Featured with excellent optical properties and biocompatibility, various coumarin-based fluorescent probes have been developed.In this work, with coumarin as the fluorescent group and monocyanovinyl recognition group, we presented an organic small molecule-based fluorescent probe featured with good water solubility for simultaneous detection of hydrazine and viscosity. N_2H_4-induced removal of electron withdrawing moiety would affect the electron density distribution, leading to N_2H_4-dependent green fluorescence enhancement response of the probe with detection limit of as low as 0.135 μM, this probe could be used for vapor N_2H_4 detection in colorimetric and fluorescent manners. In addition,the probe demonstrated viscosity-dependent fluorescence enhancement behavior, in aqueous solution with high viscosity, the free rotation of the probe would be dramatically inhibited, which affects the distortion of intramolecular charge transfer (ICT) and thus leads to red fluorescence enhancement of the probe, and as high as 150-fold enhancement could be obtained at 95% glycerol aqueous solution. In addition to N_2H_4 vapor detection in colorimetric and fluorescent manners, cell imaging experiment revealed that the probe could be used for the discriminating of living and dead cells, demonstrating the potential in the revealing of the occurrence and development of diseases.

Assessing Myriocin and NAC for protection against cisplatin induced hearing loss and renal toxicity in Mice

Zhiyi Liu[1] （刘治义）, Lin Cheng[2] , Ke Liu[1*]

[1]*Key Laboratory of Bio-Resources and Eco-Environment of Ministry of Education, College of Life Science, Sichuan University, 610065, Chengdu China*

[2]*State Key Laboratory of Biotherapy, Sichuan University, 610041, Chengdu China*

**Correspondence email: kliu@scu.edu.cn*

Abstract

Cisplatin, an antitumor drug, is widely used in the treatment of solid tumors. However, cisplatin chemotherapy can cause permanent hearing loss in 40% to 60% of cancer patients, and cisplatin therapy can also cause severe renal toxicity as a side effect, thereby limiting its use. The antioxidant n-acetylcysteine (NAC) has been shown in clinical trials to have an ear-protective effect in patients with tumors treated with cisplatin, and no serious consequences have occurred after NAC treatment, making it a promising compound for the treatment of cisplatin-induced hearing loss. Myriocin is a fungal metabolite that has the potential to inhibit tumor growth and regulate REDOX homeostasis.

Here, a mouse model of cisplatin-induced hearing loss was constructed through multi-cycle low-dose intraperitoneal injection, in which a dose of 3 mg/kg cisplatin was injected twice a week for 6 weeks, more closely resembling the type and extent of clinically observed hearing loss. We used C57BL/6J mice and divided them into control, Myriocin, NAC, and Myriocin-NAC groups. The protective effect of Myriocin and NAC against cisplatin was determined by functional hearing tests (ABR), external cochlear hair cell counts, and pathological assessments of the kidneys of different groups of mice.

The results showed that after cisplatin modeling, the control and Myriocin-treated mice displayed significant hearing loss at all test frequencies, whereas the low-frequency hearing loss was not significant in the NAC and Myriocin-NAC dual treatment groups. Both NAC and Myriocin reduced cisplatin-induced weight loss.

In conclusion, this study demonstrates that NAC has a protective effect against cisplatin-induced hearing loss at low frequencies, whereas the protective effect of Myriocin is not particularly significant. Additionally, both NAC and Myriocin can reduce the weight loss caused by cisplatin treatment and mitigate the side effects of cisplatin therapy. Furthermore, Myriocin may exhibit a protective effect against cisplatin-induced renal toxicity in mice. Future studies will focus on the biochemical analysis of each group, the evaluation of hair cell numbers in the cochlear basement membrane of mice in each group, and further complementary cell experiments to explore the molecular mechanism of NAC and Myriocin in the treatment of cisplatin ototoxicity.

Dimethyl α-Ketoglutarate Promotes the Synthesis of Collagen and Inhibits Metalloproteinases in HaCaT Cells

Bo-Yeong Yu[1] and Young-Sam Keum[1*]

[1]*College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University, Goyang 10326, Korea*

**Correspondence email: bo073@naver.com*

Abstract

Reactive oxygen species (ROS) cause skin aging. Excessive oxidative stress causes collagen and elastin chain scission and abnormal cross-linking, which leads to wrinkles. We observed that treatment with dimethyl α-ketoglutarate (DMK) increased the amount of intracellular α-ketoglutarate significantly more than that of α-ketoglutarate in HaCaT cells. DMK also increased the level of intracellular 4-hydroxyproline and promoted the production of collagen in HaCaT cells. In addition, DMK decreased the production of collagenase and elastase, and downregulated the expression of selected matrix metalloproteinases (MMPs), such as MMP-1, MMP-9, MMP-10, and MMP-12 via transcriptional inhibition. The inhibition of MMPs by DMK was mediated by suppressing the interleukin-1 (IL-1) signaling cascade, leading to the attenuation of ERK1/2 phosphorylation and AP-1 transactivation. Our study results illustrate that DMK, an alkylated derivative of α-ketoglutarate, increases the level of 4-hydroxyproline, promotes the production of collagen, and inhibits the expression of selected MMPs by affecting the IL-1 cascade and AP-1 transactivation in HaCaT cells. The results suggest that DMK might be useful as an anti-wrinkle ingredient.

Dynamic proteostasis imbalance is a hallmark of aging

Chang Shi[1,2]（时畅）, Xinhua Qiao[1], Ting Xie[1,2], Yuanyuan Wang[1], Chang Chen[1,2*]

[1]Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101; [2]University of Chinese Academy of Sciences, Beijing 100049

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Background: The imbalance of proteostasis will accelerate aging, and loss of proteostasis is a hallmark of aging, but there is little research on the dynamic characteristics of proteostasis during aging, let alone its mechanism.

Methods: In our study, human dermal fibroblasts(HDF) was selected as replicative senescent cell models. We performed real-time imaging and other quantitative experiments to systematically detect the rate of protein synthesis, refolding, trafficking, degradation, ER UPR and mtUPR in young and senescent cells.

Results: We found that the total amount of newly synthesized proteins in senescent cells is lower than that in young cells after puromycin treatment. The protein refolding rate in senescent cells is also lower detected by sf roGFP probe and J chain experiment. The increase rate of sXBP1/total XBP1 in senescent cells is lower than that in young cells under ER stress. Moreover, proteins transported from ER to Golgi in young cell is faster than senescent cells detected by RUSH system. Mechanically, redox environment metabolomic evaluation (REME) showed that arginine, citrulline and iNOS levels increased in senescent cells. Quantitative *S*-nitrosation proteomic analysis showed that the *S*-nitrosation level of 18 proteins related to protein synthesis, refolding, trafficking and degradation increased in senescent cells, among which, IRE1α, HSP90B1, BCAT2 and ERP44 are potential targets that causes dynamic proteostasis imbalance in aging.

Conclusion and significance: This study focused on the dynamic rate of proteostasis during cell senescence based on real-time detection, and showed that dynamic proteostasis imbalance is a hallmark of cell senescence. We will perform experiments to verify that dynamic proteostasis imbalance is caused by protein *S*-nitrosation, and try to provide a new strategy for healthy aging.

Key Words: dynamic proteostasis, cell senescence, *S*-nitrosation

Increasing redox-stress signaling threshold (RST) through stress to delay aging

Haoyang Shi[1,2] （时浩洋）, Meng Jiao[1] , Chang Chen[1,2*]

1Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing, 100101, China; 2University of Chinese Academy of Sciences, Beijing 100049, China

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Background:In recent years, various studies revealed that oxidative stress exhibits a dual effect that functions physiologically at a low concentration and induces pathological damage at high levels. However, the antioxidant strategies for anti-aging still focus on repairing after the oxidative damage. In our previous study, we defined Redox-stress Signaling Threshold (RST), below which redox stress had benefits. We demonstrated that through the stress stimulation, RST increased accompanied by the delayed aging process (*Free Radic Biol Med*. 2021). On this basis, we proposed a new hypothesis that RST can be actively increased through applying appropriate stress to prevent damage and achieve delayed aging.

Methods: In this study, we applied the fasting as a stress stimulation in *C. elegans* to figure out the way to increase RST. The fasting stress was applied during the early, mid-life or elder stage of *C. elegans* to investigate if the duration of stress is an important factor to RST and what is the beneficial time window.

Results: Applying the fasting during the early stage, we observed an increasing trend of RST. A less increased RST was identified when applied the stress during mid-life. However, when we performed the fasting during elder stage, the RST was reduced.

Discussion: These results suggest the existence of a time window for application of stress that corresponds to the enhancement of RST and delayed aging. For *C. elegans*, the time window seems to be early and mid-life. These efforts built a basis for further study on elevating RST. In the future, we will continue to explore the intensity of stress and other stress factors, hoping to provide a novel active health strategy to delay aging by autonomously preventing oxidative damage formation.

Key Words: Redox, Oxidative stress, aging, RST, antioxidant

Inhibition of ER Stress as a Protective Strategy of 3,3',4',5,5',7 Hexahydroxyflavone against PM2.5-induced Apoptosis in Skin Cells

Herath Mudiyanselage Udari Lakmini Herath, Mei Jing Piao, Kyoung Ah Kang, Pincha Devage Sameera Madushan Fernando, Jin Won Hyun

Department of Biochemistry, College of Medicine and Jeju Research Center for Natural Medicine, Jeju National University, Jeju 63243, Republic of Korea

**Correspondence email: lakminiherath91@gmail.com*

Abstract

Epidemiological research has well-documented the effects of particulate matter 2.5 ($PM_{2.5}$) on the skin, including aging, irritation, and disruption of homeostasis. This study investigated the effects of 3,3',4',5,5',7-hexahydroxyflavone (HHF) on skin damage caused by $PM_{2.5}$. HaCaT keratinocytes were pretreated with HHF and then exposed to $PM_{2.5}$ for 24 hours. The results showed that $PM_{2.5}$ increased reactive oxygen species (ROS) production, leading to DNA damage, lipid peroxidation, protein carbonylation, and cell death. However, HHF reduced these effects. Endoplasmic reticulum (ER) stress-related protein activation by $PM_{2.5}$ indicated that $PM_{2.5}$-induced ER stress. ER stress inhibitor further confirmed the ER stress-related increases in cell death and apoptosis, which HHF mitigated. Additionally, HHF reduced mitochondrial damage and activation of the MAPK signaling pathway caused by $PM_{2.5}$. Enhancement of cell viability and reduction of cellular apoptosis level was observed when both HHF and MAPK inhibitors were treated with $PM_{2.5}$. Thus, HHF may be useful for ameliorating the skin damage caused by $PM_{2.5}$ as it reduces ROS, ER stress, mitochondrial damage, and apoptosis by downregulating the MAPK signaling pathway (RS-2023- 00270936).

Key Words: $PM_{2.5}$, 3,3',4',5,5',7-Hexahydroxyflavone, ER stress.

Optimization of Brain Microvascular Endothelial Cell Extraction

Ruikun Xie（谢睿坤）, Yanzhong Chang

Hebei Normal University

**Correspondence email: xrk8023@163.com*

Abstract

The blood-brain barrier is a critical barrier that regulates the entry and exit of substances in the brain.The brain microvascular endothelial cells (BMECs) are a key component of this barrier. Therefore, BMECs are important subjects of research in stroke and neurodegenerative diseases. To investigate the underlying molecular mechanisms, it is necessary to isolate and purify endothelial cells and then measure various indicators that reflect molecular changes in the brain microvasculature. Current methods for isolating brain microvasculature include dextran separation and sucrose separation, with density gradient and differential centrifugation being the key steps in these processes. Additionally, research has shown that dextran has a certain affinity for specific molecules on brain microvessels and can even be used for drug targeting. In light of this, we utilized this property to explore the dextran separation method. Before the centrifugation, we mixed brain homogenates with dextran solution at room temperature and 4℃ temperature for different time. We found that mixing for 30-60 minutes at 4℃ temperature conditions resulted in the best purification for the brain microvascular cells, with relatively minimum contamination from other tissues. It is suggested that this condition, which minimizes material degradation, may facilitate sufficient interaction between dextran and brain microvessels, thereby enhancing the thoroughness of subsequent separation and purification processes, making the measured indicators more reliable. The optimization of this purification method can promote the study of the molecular mechanisms of related diseases across the blood-brain barrier and the redox reactions involved, which is of considerable significance.

Key Words: Blood brain barrier,Brain microvascular endothelial cells,Purification

Quercetin 3-D-galactoside mitigates PM2.5-mediated keratinocyte cell senescence by alleviating the endoplasmic reticulum and mitochondrial stress

Pincha Devage Sameera Madushan Fernando, Mei Jing Piao, Herath Mudiyanselage Udari Lakmini Herath, Kyoung Ah Kang, and Jin Won Hyun

Department of Biochemistry, College of Medicine, and Jeju Research Center for Natural Medicine, Jeju National University, Jeju 63243, Republic of Korea

**Correspondence email: sameeramadhu91@gmail.com*

Abstract

Quercetin 3-D-galactoside (Q3G), a natural compound belongs to the class of flavanol glycosides, which is considered a potential candidate to mitigate the risk of diseases associated with oxidative stress as well as exhibit anticancer properties. The particulate matter 2.5 ($PM_{2.5}$) causes skin inflammation, aging, and skin barrier dysfunction, also respiratory and cardiovascular diseases. The presence study was focused on assessing the therapeutic potential of Q3G against $PM_{2.5}$- mediated keratinocyte cell damage. Through the initial assessments, Q3G-exhibited strong antioxidant and cytoprotective ability against $PM_{2.5}$ exposure. Western blotting evaluation revealed that Q3G mitigated the $PM_{2.5}$-mediated endoplasmic reticulum (ER) stress and mitochondria damage. Additionally, Q3G inhibited the activation of ER stress-related proteins activated by $PM_{2.5}$, and also Q3G alleviated $PM_{2.5}$-induced excessive mitochondrial Ca^{2+} and mitochondrial reactive oxygen species generation. The colony formation evaluation and assessment of cell cycle progression revealed that Q3G could restore $PM_{2.5}$-impaired cell proliferation, additionally, Q3G enhanced the $PM_{2.5}$-mitigated G_0/G_1 phage regulatory proteins. Q3G-markedly decreased the levels of matrix metalloproteinases (MMPs), and senescenceassociated β-galactosidase, those elevated by $PM_{2.5}$. In conclusion, Q3G alleviates $PM_{2.5}$-mediated ER and mitochondrial damage, and MMPs expression, and restores $PM_{2.5}$-impaired cell proliferation, which indicates Q3G is a potential therapeutic candidate against $PM_{2.5}$-mediated skin damage (RS-2023-00270936).

Key Words: Quercetin 3-D-galactoside, $PM_{2.5}$, ER stress, Mitochondria damage

Relationship between ferroptosis and cellular senescence caused by particulate matter 2.5 in skin keratinocytes

Mei Jing Piao, Kyoung Ah Kang, Pincha Devage Sameera Madushan Fernando, Herath Mudiyanselage Udari Lakmini Herath and Jin Won Hyun

College of Medicine, and Jeju Natural Medicine Research Center, Jeju National University, Jeju 63243, South Korea

**Correspondence email: mjpiao@jejunu.ac.kr*

Abstract

The skin, the largest organ in the human body, which is most exposed to external pollutants, is easily damaged by particulate matter (PM) in the air. There are various mechanisms of skin cell damage caused by PM, and it has recently been reported that ferroptosis is also involved. Additionally, although there are reports that exposure to PM accelerates cellular senescence, there are no reports on the relationship between PM-induced ferroptosis and cellular senescence. 20 μg/cm2 of $PM_{2.5}$, a fine particle with a diameter smaller than 2.5 μm was exposed to human HaCaT keratinocytes, and ferroptosis or cellular senescence-related characteristics were confirmed through experimental techniques such as flow cytometry, confocal microscopy, western blot, and immunochemical analysis. After $PM_{2.5}$ treatment, decreased cell viability via calcein-AM fluorescent reagent staining; production of large amounts of intracellular reactive oxygen species through staining with H2DCFDA fluorescent reagent; formation of lipid peroxidation through staining with BODIPY^{TM} 581/591 C11, a lipid peroxidation sensor; reduction of labile ferrous (Fe^{2+}) ions through BioTracker FerroOrange live cell dye; a decrease in SLC7A11 and GPX4 protein expressions were confirmed. These changes were significantly reduced by the ferroptosis inhibitor. These results proved that ferroptosis is also involved in the skin cell damage mechanism caused by $PM_{2.5}$. In addition, it was confirmed that changes such as increased senescence-associated β-galactosidase activity, G_1 phase cell cycle arrest, and increased expression of aging-related proteins due to $PM_{2.5}$ treatment were significantly reduced by ferroptosis inhibitor. These results suggest that ferroptosis may be one of the causes of cellular senescence caused by $PM_{2.5}$ exposure (RS-2023-00270936).

Key Words: particulate matter, reactive oxygen species, ferroptosis, cellular senescence.

The modification of 8-oxyguanine in the microRNA seed region regulates aging process

Jiaqi Guo[1,2]（郭佳琪）, Yingmin Zhang[1], Qing-Yu Wang[1,3], Huan Xi[1], Jianping Cai[1]

[1] *The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital/National Center of Gerontology of National Health Commission, Beijing, China, 100730.*

[2] *University of Chinese Academy of Sciences, Beijing, China, 100049.*

[3] *Medical Research Center, Beijing Institute of Respiratory Medicine and Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China, 100020.*

**Correspondence email: xih@bjhmoh.cn; caijp61@vip.sina.com*

Abstract

In the aging process, the expression of P16, P21 and P53 increases, while the level of reactive oxygen species also raises. Recent studies have found that RNA is more susceptible to oxidation than DNA, and the existence of oxidative miRNA and their effects in cardiac hypertrophy and tumors have been verified. Therefore, we explored whether oxidative miRNAs can regulate aging process. Through miRNA database screening, oxidative miRNA sequencing and in vitro validation, we identified two miRNAs, miR-3118 and miR-134-5p, which could inhibit the expression of P16 by binding to the 3'-UTR of P16 mRNA, thereby promoting the cell cycle to delay aging. Meanwhile, miR-3118 and miR-134-5p can also affect the aging process by regulating anti-aging proteins, autophagy and apoptosis. When the guanine of miRNA seed region was oxidized to oxyguanine(o8G-miRNA) or mutated to uracil(U-miRNA)(G→o8G/U, pairs with base adenini), the inhibitory effect of miR-3118 or miR-134-5p on P16 was reduced to different degrees. The results of RNA-Seq showed that oxidative miRNA can promote aging by regulating some new target genes which are also related to aging or cell cycle. At the same time, the effect of oxidative miRNA on promoting aging was also verified in C57BL/6J mice. In summary, we have discovered the role of oxidative miRNAs in the aging process, which may provide new therapeutic targets for anti-aging and aging-related diseases.

Key Words: microRNA; 8-oxyguanine; P16; Aging

Txn1-F54L mutation in rats generates neurodegeneration and chronic kidney disease through mitochondrial dysfunction and multiple cell death modes

Iori Ohmori

Faculty of Education, Department of Child Neurology, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Shikatacho 2-chome 5-1, Kita-ku, Okayama 700-8558, Japan.

**Correspondence email: iori@md.okayama-u.ac.jp*

Abstract

Thioredoxin 1 (Txn1) is one of the enzymatic antioxidants that regulate redox balance. In humans, thioredoxin has been identified in the culture media of adult T-cell leukemia cell lines. However, few studies have investigated the role of thioredoxin in vivo. Recently, we discovered a strain from the Kyoto University archive that harbors a chemically induced *Txn1*-F54L mutation in rats with running seizures. This study aimed to elucidate the function of *Txn1*-F54L, the phenotype of the rats, and the underlying pathophysiology of this rat. The insulin-reducing activity of *Txn1*-F54L was approximately one third of that of the wild type (WT). TUNEL assay showed that fibroblasts derived from homozygotes were susceptible to cell death under oxidative stress. Bilateral symmetric vacuolar degeneration in the midbrain was observed in *Txn1*-F54L rats. The lesions showed neuronal cell death. Neurons in *Txn1*-F54L rats showed morphological changes in the mitochondria. Laboratory tests and pathological examinations were performed on WT rats and rats with homozygous *Txn1*-F54L mutations. *Txn1*-F54L mutant rats exhibited progressive albuminuria, hypoalbuminemia, and hypercholesterolemia. Renal pathology revealed marked nephrosclerosis, tubular dilatation, interstitial fibrosis, and decreased mitochondrial number, especially in the proximal tubules. Our results suggest that the Txn1 mutation causes chronic kidney disease (CKD) in rats. Bulk RNA-seq of the kidney showed significant upregulation of genes associated with pathogen-induced cytokine storm signaling pathway. These genes are involved in several regulated cell death pathways such as pyroptosis, apoptosis and necroptosis in mutant rats. Our studies have shown that reduced thioredoxin function leads to neurodegeneration and chronic kidney disease in vivo. Multiple cell death pathways were involved in the brain and kidney lesions.

Chemerin Activates the NLRP3 Inflammasome Through CMKLR1, Mediating Potassium Current Dysregulation and Obesity-Related Atrial Fibrillation

Yating Chen[1,2#]（陈雅婷）, Bin Li1,[3#], Yang Li[2*]

1. Medical School of Chinese PLA, Beijing, China

2. Senior Department of Cardiology, the Sixth Medical Center of PLA General Hospital, Beijing, China

3. Department of Emergency, the Eighth Medical Center of PLA General Hospital, Beijing, China

**Correspondence email: liyangbsh@163.com*

Abstract

Background: Obesity is an independent and significant risk factor for atrial fibrillation (AF), greatly increasing its incidence. However, the specific mechanism linking obesity to AF remains unclear. Clinical studies have indicated a strong association between abnormal adipokine levels and the development of AF. Chemerin, an adipokine, has elevated circulating plasma levels in patients with both obesity and AF. It plays roles in chemotactic recruitment of inflammatory factors and metabolic regulation, primarily exerting its biological effects through CMKLR1. In this study, we selected Chemerin as a key molecule to investigate the pathogenesis of obesity-related atrial fibrillation and explore its potential mechanisms in AF development.

Objective： To investigate how Chemerin activates the NLRP3 inflammasome and other related inflammatory factors via CMKLR1, leading to abnormal potassium currents and the onset of obesity-related AF.

Methods: The dataset (GSE32095) from high-throughput sequencing of epididymal adipose tissue in obese and control mice, available in the NCBI GEO database, was used for differential gene expression, cluster analysis, GO and KEGG enrichment analysis. Adipokines and potential mechanisms involved in the development of obesityrelated AF were identified. C57BL/6J mice were divided into high-fat diet (HFD) group and low-fat diet (LFD) group. AF was induced by

transesophageal atrial pacing, and induction rates were compared between the two groups. Atrial myocytes were acutely
isolated, and action potentials (AP), Ito and IKUr currents were recorded by patch-clamp technique. Expression levels of potassium-related channel proteins, NLRP3, and other inflammatory factors in atrial tissue were measured via Western blot.

Results: (1) Chemerin derived from adipocytes is a key molecule mediating the effects of adipocytes on atrial cells. (2) The incidence of AF significantly increased in the HFD group. (3) The action potential duration (APD50 and APD90) of atrial myocytes in the HFD group was shortened. (4) The Ito and IKUr current densities in atrial myocytes of the HFD group increased significantly, from 19.46±0.84 pA/pF to 31.14±1.00 pA/pF and from 11.44±0.95 pA/pF to 18.21±0.58 pA/pF, respectively ($n=10$, $P<0.05$). (5) Gating mechanism studies show that, compared to LFD group, the steady-state activation curve of Ito in atrial myocytes from obese mice shifted leftward, the steady state inactivation curve shifted rightward, and the recovery curve after inactivation shifted upward, indicating increased Ito channel activation and decreased inactivation at the same voltage in obese mice. Recovery after inactivation was also accelerated, promoting increased Ito current density due to more effective channels. (6) Levels of NLRP3, Pro-Casp1, P20, IL-18, IL-1β, and IL-1β spliceosomes were all elevated in the HFD group.

Conclusions: The induction rate of AF is significantly higher in obese mice, accompanied by increased Ito and IKUr currents in atrial myocytes and upregulation of NLRP3 and other inflammatory factors. This may be driven by elevated Chemerin secretion in obese mice, which activates NLRP3 and related inflammatory pathways via CMKLR1, leading to shortened action potential duration, enhanced reentry, and the onset of AF.

Key Words: Atrial fibrillation, Obesity, Chemerin, NLRP3 inflammasome, Potassium channels

Different roles of E-prostanoid 3 receptor on renal parenchymal cells and myeloid cells in acute oxalate nephropathy

Jinwei Guo[1,2]（郭锦伟）, Yingbi Zhou[2#] Bin Liu[1,2#],

[1]*Cardiovascular Research Center, Shantou University Medical College, 22 Xin-Ling Rd, Shantou, 515041 China;*

[2]*Guangdong Provincial Key Laboratory of Infectious Diseases and Molecular Immunopathology, Shantou University Medical College, 22 Xin-Ling Rd, Shantou, 515041 China;*

**Correspondence email: jw861630056@outlook.com*

Abstract

BACKGROUND: Prostaglandin E_2 is widely involved in the progression of inflammatory diseases through E-prostanoid 3 receptor (EP3). In addition, the receptor in renal parenchymal cell also participates in water and salt metabolism. However, how EP3 affects the progression of acute oxalate nephropathy is still unknown.

METHODS: Experiments were performed with WT, global *Ep3* knockout (*Ep3*$^{-/-}$) and myeloid cell-conditional *Ep3*knockout (*Ep3*$^{F/F}$*;Lyz2*^{Cre}) mice. Acute oxalate nephropathy model was established by intraperitoneally injecting 1% sodium oxalate solution (100mg/kg) and giving 3% sodium oxalate solution as drinking water. Indicators of renal injury or inflammation were detected by HE, ELISA, immunofluorescence, WB, and RT-qPCR.

RESULTS: Deficiency of EP3 on myeloid cells led to decreased renal injury indicators, neutrophil infiltration and chemokines expression levels in mice. In addition, we observed that the expression or activation of apoptosis, necroptosis and pyroptosis related proteins were reduced in *Ep3*$^{F/F}$*;Lyz2*^{Cre} mice. However, *Ep3*$^{-/-}$ mice showed no signs of improved renal function, with increased renal calcium oxalate crystal content. Compared with those in WTs, urine volume and urinary oxalate content in *Ep3*$^{-/-}$ mice were reduced and the expression of SLC26a6 was increased.

CONCLUSIONS: Our study demonstrates that deficiency of EP3 on myeloid cells blocks necroinflammation by reducing inflammatory responses and hence renal cell death to effectively improve acute oxalic nephropathy. Meanwhile, deficiency of EP3 on parenchymal cells results in decreases in both urine and oxalate excretions, which may lead to the ineffectiveness of global abrogation of EP3.

Key Words: prostaglandin E_2; EP3; acute oxalate nephropathy; inflammation; oxalate excretion

Dysregulated peroxisomal metabolites in cardiac adipose tissue induce heart dysfunction

Se Jin Jung2† , Gahee Song1† , Wenjun Jiao2†, Woo Yong Park1 , Yunju Jo4 , Ja Yeon Park2 , In Jin Ha3 , Dongryeol Ryu4 , Kuk Hui Son5*, Hyun Jeong Kwak6*, and Jae-Young Um1,2*

1.Department of Pharmacology, College of Korean Medicine, Kyung Hee University, Seoul 02447, Republic of Korea

2.Department of Science in Korean Medicine, Graduate School, Kyung Hee University, Seoul 02447, Republic of Korea

3.Korean Medicine Clinical Trial Center (K-CTC), Kyung Hee University Korean Medicine Hospital, Seoul, 02447, Republic of Korea

4.Department of Biomedical Science and Engineering, Gwangju Institute of Science and Technology, Gwangju, 61005, Republic of Korea

5.Department of Thoracic and Cardiovascular Surgery, Gachon University Gil Medical Center, Gachon University, Incheon 21565, Republic of Korea

6.Department of Bio and Fermentation Convergence Technology, Kookmin University, Seoul, 02707, Republic of Korea

**Correspondence email: sejin9135@gmail.com*

Abstract

Adipose tissue is an important regulator of cardiovascular disease by secreting bioactive products, including adipocytokines, microvesicles, and inorganic molecules. In particular, the browning of cardiac adipose tissue (CAT), including perivascular adipose tissue (PVAT) and epicardial adipose tissue, directly affects the adjacent cardiac vascular wall or myocardium, but its detailed mechanisms remain incompletely understood. Here, we established model of cardiac hypertrophy, fibrosis, and whitening of CAT, by feeding a high-fat diet (HFD) to mice. Obesity altered the profile of free fatty acid (FFA) metabolites in CAT, particularly reducing phytanic acid peroxisomal oxidation in PVAT. Additionally, the PVAT of obese mice showed a significant decrease in peroxisomal membrane proteins or peroxin (including PEX13, PEX14, and PEX16), peroxisomal acyl-coenzyme A oxidase 1 (ACOX1), and peroxisome proliferator-activated receptor alpha (PPARα). Furthermore, we induced peroxisome dysfunction in adipocytes using Mdivi-1 and 10,12-tricosadiynoic acid. Peroxisome dysfunction decreased catalase activity and increased ROS levels. Also, H9C2 cardiomyocytes treated with conditioned medium from peroxisomal dysfunction adipocytes showed hypertrophy and fibrosis. Taken together, dysregulated FFA due to peroxisome dysfunction inhibit browning of CAT and leads to causes cardiac dysfunction. Therefore, targeting cardiac adipose tissue remodeling by modulating peroxisome function will expand the paradigm of cardiovascular disease treatment.

Key Words: Heart dysfunction, Obesity, Cardiac adipose tissue, Browning, Peroxisome, Reactive Oxygen Species

GSNOR contributes to age-related obesity by regulating the S-nitrosation of Beclin-1 to promote adipose tissue whitening

Ting Xie [1,2]（谢婷）, Xinhua Qiao [1], Chang Chen [1,2*]

[1] *Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China.*
[2]*University of Chinese Academy of Sciences, Beijing, 100049, China.*

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Obesity is the most common medical condition in middle age, however, the underlying mechanisms remain poorly defined. Herein, we report that *S*-nitrosoglutathione reductase (GSNOR), a key enzyme in the regulation of *S*-nitrosation, increases significantly in inguinal white adipose tissue (iWAT) of naturally aging mice and humans. GSNOR knockout (KO) mice exhibit leaner, less adipose tissue and increase thermogenesis after middle age. While adipose tissue-specific overexpressed GSNOR (GSNOR KI) mice are fatter and decline thermogenic function. We discover that GSNOR KO mice have more beige adipocytes and higher mitochondria levels in iWAT. We identified *S*-nitosation of Beclin-1, a core member of autophagy, is the key target of GSNOR employing *S*-nitrosation proteomics, and the *S*-nitrosation of Beclin-1(C351) is responsible for the maintenance of mitochondria level and browning adipocytes by weakening autophagy. Further study shows that Beclin-1^{C351A} increases autophagy initiation of iWAT by enhancing the interaction with ATG14, accelerates clearance of mitochondria, and promotes adipose tissue whitening. Surprisingly, the age-related increase in weight of iWAT was salvaged by knocking down GSNOR in vivo. In conclusion, this study demonstrates that GSNOR promotes adipose tissue whitening in age-related obesity by denitrosation of Beclin-1, which provides a new direction for the control of aging-associated obesity and metabolic disorders.

Key Words: GSNOR, age-related obesity, adipocytes whitening, Beclin-1, *S*-nitrosation/*S*-nitrosylation, autophagy

Short CV

Name: Tie Xie, PhD Candidate, Institute of Biophysics, Chinese Academy of Sciences. Date of Birth: June 1, 1996. She has published 2 SCI articles as the first author or co-first author in the journals Nitric Oxide and Progress in Biochemistry & Biophysics.

Hepatic Adenosine Kinase mitigates hepatic steatosis and insulin resistance in obese mice

Kai Luo（骆开）

Chinese Academy of Sciences College of Life Sciences

**Correspondence email: luokai20@mail.ucas.ac.cn*

Abstract

Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease characterized by hepatic fat deposition, and is often accompanied by obesity, insulin resistance, dyslipidemia and other metabolic disorders. Adenosine kinase (ADK) is a phosphotransferase that phosphorylates adenosine to adenosine monophosphate (AMP). ADK-deficient patients suffer from severe hepatic dysfunction and hepatic steatosis. However, the underlying mechanisms remain poorly understood. Here, we found that the ADK inhibitor ABT-702 alleviated hepatic steatosis in leptin-deficient mice. We further investigated mice with hepatocyte-specific ADK disruption and overexpression. Unexpectedly, hepatocyte-specific disruption of ADK exacerbated hepatic steatosis, insulin resistance, and hepatic inflammation. In contrast, mice with hepatocyte-specific ADK overexpression exhibited decreased hepatic fat deposition and inflammation. Mechanistically, hepatocyte-specific ADK disruption upregulated the activities of NF-kappaB p65 and MAPK signaling pathways. Furthermore, hepatocyte ADK disruption at different stages of high-fat diet revealed that hepatocyte ADK exacerbated lipid deposition by decreasing PPARα-regulated fatty acid β-oxidation gene expression at early stages, and further exacerbated NAFLD progression through inflammatory responses and oxidative stress in advanced stages. Therefore, hepatocyte ADK is a therapeutic target for the treatment of obesity and NAFLD.

Inhibition of GCN2 alleviates hepatic steatosis and oxidative stress in alcoholic-related liver disease

Ying Xu（徐颖）

College of Life Science, University of Chinese Academy of Sciences, Beijing, 100049, China.

**Correspondence email: xuying162@mails.ucas.ac.cn*

Abstract

Globally, excessive alcohol consumption stands as a prominent etiological factor for alcohol-related liver disease(ALD), significantly contributing to the burden of chronic liver disease and posing a considerable risk for cardiovascular complications and indications for liver transplantation. However, the development of effective pharmacological therapies for ALD remains an unmet need. Drawing upon our prior research, we established that GCN2 inhibition mitigated liver steatosis and oxidative stress in non-alcoholic fatty liver disease(NAFLD).In this study, we extend our observations to demonstrate that GCN2 knockout effectively alleviated liver steatosis, oxidative stress, and inflammatory responses in ALD. Notably, administration of specific GCN2 inhibitors at varied concentrations resulted in mitigated hepatic tissue damage, decreased lipid deposition, attenuation of inflammation, and enhancement of mitochondrial function. Transcriptomic profiling highlighted peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC1-α) as a pivotal regulatory element.Further, treatment with GCN2 inhibitor elicited upregulation of SIRT1, PGC1-α, and PPARα expression in the livers of treated mice, suggesting a potential mechanism whereby GCN2 inhibitors may activate downstream fatty acid oxidation pathways by mitigating the suppressive effects of alcohol on SIRT1, ultimately influencing mitochondrial biogenesis. These findings underscore the therapeutic potential of GCN2 inhibitors in the management of ALD and warrant further exploration.

Intestinal flora-bile acid-FXR axis regulates hepatic lipid metabolism induced by arsenic and fluoride co-exposure in rats

Jinyao Chen[1]（陈锦瑶）, *Qiang Su, Xiaoyan Yan*

School of Public Health, Shanxi Medical University, Taiyuan 030001, Shanxi

Correspondence email: kamuichan@126.com1, yanxiaoyan@sxmu.edu.cn

Abstract

Background The mammalian gut microbiome (GM) plays a critical role in fluoride and arsenic exposure induced hepatic toxicity. Intestinal bile acid metabolism has been shown to influence hepatic lipid metabolism, but to our knowledge its role in fluoride and arsenic alone and combined exposure is largely unknown.

Methods We established fluoride and/or arsenic exposure model from pregnancy to 120 days after birth by drinking water and administrated fecal microbiota transplantation (FMT) to conventionally raised (with normal microbiomes) and combined exposure (with poisoned microbiomes) rats to investigate the regulatory effect in hepatic-lipid metabolism and its toxicity.

Results Lipid metabolism was disturbed in liver and serum after exposure, while serum total bile acids (TBA) levels were elevated in rats after arsenic and fluoride exposure, and the bile acid pool was altered. Levels of CDCA, 7-CDCA, 12-KDCA, GUDCA, DCA, and UCA were increased, and GCA and GDCA were decreased. The protein expression of FXR and FGF15 in colon, and FXR, FGF15, FGFR4, SHP and BSEP in liver were reduced. Meanwhile, CYP7A1 and CYP8B1 were increased in each of the dyed groups. It also revealed a decrease in lipid β-oxidation protein expression, including PPARα and PGC1α, and an increase in lipid synthesis protein PPARγ in the liver of all exposure groups. Besides, metabolomics discovered that poisoning significantly perturbed the gut microbiome composition, and the characterized species were screened. After bidirectional FMT, liver injury recovered by transplanting healthy microbiomes and aggravated by transplanting co-exposure microbiomes. The same results were found in serological indicators and metabolomics.

Conclusions Long-term exposure of arsenic and fluoride could generate intestinal damage and liver toxicity by regulating circulating metabolites by disruption of the “liver-intestinal” cycle. FXR axis may be the key mechanism of arsenic and fluoride-induced disorder of hepatic lipid metabolism.

Key Words: Arsenic, Fluoride, Liver, Bile acid, FXR, Lipid metabolism

Knocking out GCN2 exacerbates oxidative stress in the liver under zinc-deficient conditions by reducing Nrf2 expression

Zhuoran Yu（于卓然），Zhongbing Lu.

College of Life Sciences, University of Chinese Academy of Sciences, Beijing 100049, China;

**Correspondence email: yuzhuoran19@mails.ucas.ac.cn; luzhongbing@ucas.ac.cn*

Abstract

Zinc deficiency is currently one of the health risk factors faced by the global population. The oxidative stress and lipid accumulation in the liver induced by zinc deficiency are significant factors that contribute to the development of non-alcoholic fatty liver, cardiovascular diseases, and diabetes. Previous studies have indicated that under conditions of CCl4-induced liver injury and hepatic lipid deposition, inhibition of general control nonderepressible 2 (GCN2), a sensor of amino acid availability, can alleviate liver oxidative stress by upregulating Nrf2 expression.In this study, we found that in mice fed with a zinc-deficient diet, the knockout of GCN2 reduced the expression of Nrf2 and its downstream antioxidant proteins HO-1 and NQO-1,along with an increase in reactive oxygen species levels in the liver. However, hepatic-specific overexpression of the zinc transporter ZIP4 or intraperitoneal ZnCl2 injection reduced oxidative stress in the liver of $Gcn^{2-/-}$ mice. Additionally, $Gcn^{2-/-}$ mice on a zinc-deficient diet exhibited significantly exacerbated liver damage and increased oxidative stress following CCl4 injection, while the expression of Nrf2 ,HO-1 and NQO-1 were decreased in the liver. These results indicate that the regulatory effect of GCN2 on Nrf2 is dependent on zinc ion levels; under zinc deficient, GCN2 knockout exacerbates oxidative stress levels in the liver. Our Study is the first to demonstrate that GCN2 regulates hepatocyte redox homeostasis by sensing changes in zinc ion concentration. It also shows that under zinc deficiency conditions, GCN2 maintains hepatic zinc ion, lipid and redox homeostasis.

Machine learning based model for predicting coronary heart disease using dynamic triglyceride-glucose index: a Longitudinal study cohort CHARLS database

Yi Yang[1#]（杨易）, Zengao Yang[2, 3#], Honghong Zhang[2, 4#], Haijing Zhao[2, 4], Yue Zhu[2, 4], Yuhan Ma[2], Yuqi Liu[2,6, 7, 8*]

[1] *I.T. Department of Faculty of Engineering and Information Technology of university of technology Sydney, Australia*

[2] *Department of Cardiology, the Sixth Medical Centre, Chinese PLA General Hospital, Beijing, 100037, P.R. China*

[3] *School of Medicine, South China University of Technology, Guangzhou,510006, P.R. China*

[4] *Medical School of Chinese PLA, Chinese PLA General Hospital, Beijing, P.R. China*

[5] *Xuzhou Central Hospital, Jiangsu, 221009, P.R. China*

[6] *National Key Laboratory of Kidney Diseases, Beijing, 100853, P.R. China*

[7] *Department of Cardiology & National Clinical Research Center of Geriatric Disease, Beijing, 100853, P.R. China*

[8] *Beijing Key Laboratory of Chronic Heart Failure Precision Medicine, Beijing, 100853, P.R. China*

**Correspondence email: ametuofo980869@163.com*

Abstract

Background: Cardiovascular disease (CVD) remains a major health challenge globally, particularly in aging populations. Using data from the China Health and Retirement Longitudinal Study (CHARLS), this study examines the Triglyceride-glucose (TyG) index dynamics, a marker for insulin resistance, and its relationship with CVD in Chinese adults aged 45 and older.

Methods: This reanalysis utilized five waves of CHARLS data with multistage sampling. From 17,705 participants, 5,625 with TyG index and subsequent CVD data were included, excluding those lacking 2015 TyG data. TyG indices derived from glucose and triglyceride levels, CVD outcomes via self-reports and records. Participants divided into four groups based on TyG changes (2011-2015): low-low, low-high, high-low, high-high TyG groups

Results: Adjusting for covariates, stable high group showed a significantly higher risk of incident

CVD compared to stable low group, with an HR of 1.18 (95% CI 1.03-1.36). Similarly, for stroke risk, stable high group had a HR of 1.45 (95% CI 1.11-1.89). Survival curves indicated that individuals with stable high TyG levels had a significantly increased CVD risk compared to controls. The dynamic TyG change showed a greater risk for CVD than abnormal glucose metabolism, notably for stroke. However, there was no statistical difference in single incidence risk of heart disease between stable low and stable high group. Subgroup analyses underscored demographic disparities, with stable high group consistently showing elevated risks, particularly among <65 ys individuals, females, and those with higher education, lower BMI, or higher depression scores. Machine learning models underscored the predictive superiority of dynamic TyG over abnormal glucose metabolism for CVD.

Conclusions: Dynamic TyG change correlate with CVD risks. Monitoring these changes could predict and manage cardiovascular health in middle-aged and older adults. Targeted interventions based on TyG index trends are crucial for reducing CVD risks in this population.

Key Words: Triglyceride-glucose index; cardiovascular disease (CVD); Diabetes; Longitudinal cohort study; Insulin resistance

Nfe2l1 deficiency exacerbates alcohol-induced liver injury in mice

Jinghui Qu（曲景辉），Ruirui Wu，Xin Chen，Yongqin Xia，Xiangbo Xu，Jingbo Pi，Yuanyuan Xu*

School of Public Health, China Medical University, Shenyang, 110122

**Correspondence email: yyxu@cmu.edu.cn*

Abstract

Alcoholic liver disease (ALD) has become one of the most common chronic liver diseases in China. *Nfe2l1* and *Nfe2l2* are the same family members transcriptionally regulating multiple cellular functions, such as anti-oxidative response and proteasome activity. *Nfe2l2* has been reported to directly regulate ALDH2, an alcohol metabolism enzyme, and thus alleviate the toxic effects of alcohol. Therefore, we hypothesize that *Nfe2l1* play a role in the formation of ALD. We constructed a mouse model with hepatocyte specific knockout of *Nfe2l1* (*Nfe2l1*(L)-KO) by injecting AAV8-TBG-Cre into the tail vein of adult *Nfe2l1*-KI mice. The model showed no obvious liver damage 30 weeks after virus injection, which conquered the spontaneous liver diseases in traditional *Nfe2l1* hepatocyte knockout mice. The *Nfe2l1*(L)-KO, mice were administrated with the model of chronic and binge ethanol feeding (the NIAAA model) to study the role of *Nfe2l1* in ALD. Our results showed that compared with the control group, the alcohol group showed a significant increase in liver triglyceride content, and H&E staining results showed lipid droplet accumulation in the liver, *Nfe2l1* deficiency exacerbated liver lipid accumulation. Meanwhile, *Nfe2l1* deficiency caused changes in the expression of lipid metabolism related genes. and exacerbated the increased in serum levels in ALT and AST induced by alcohol. Liver MDA content, indicating lipid peroxidation damage, showed higher levels in the alcohol group compared to the control group, which was further increased by *Nfe2l1* deficiency. Collectively, our data suggest that *Nfe2l1* deficiency exacerbates alcoholic liver injury and lipid peroxidation.

Key Words: alcohol; alcoholic liver disease; alcoholic liver injury; NFE2L1

Obesity-induced Nox2 activation prolongs cardiac repolarization

Bin Li[1,2] （李彬）

1.The Eighth Medical Center of PLA General Hospital

2.The Sixth Medical Center of PLA General Hospital

**Correspondence email: libinlb0702@163.com*

Abstract

Obesity is associated with abnormal repolarization manifested by QT interval prolongation, and oxidative stress is an important link between obesity and arrhythmias. However, the underlying electrophysiological and molecular mechanisms remain unclear. The aim of this study is to evaluate the role of obesity in potassium current in ventricular myocytes and the potential mechanism of NADPH oxidase 2 (Nox2). We investigated the effect of Nox2 on cardiac repolarization without compromising its expression and function in other systems using mice with conditional cardiac-specific deletions of Nox2 (knockout [KO]). Wild-type, KO, and Flox littermate mice were randomized to either the control or high-fat diet (HFD) groups. Surface electrocardiograms were recorded to analyze repolarization in vivo. Whole-cell patch-clamp techniques were used to evaluate the electrophysiological phenotype of isolated myocytes in vitro. Western blotting was performed to assess protein expression levels. Compared with the control mice, the HFD group had a prolonged QTc. The consequences of an HFD were not attributed to delayed rectifier K+ and inward-rectifier K+ currents but were associated with reduced peak outward KV and fast transient outward K+ currents. Nox2-KO reversed the effect of obesity on Ipeak and Ito amplitude. Our data demonstrate that obesity mediates impaired cardiac repolarization in mice, manifested by QTc at the whole organism level and action potential duration at the cellular level, and correlated with Nox2. The electrophysiological and molecular aspects of this phenomenon were mediated by repolarizing outward K+ currents.

Key Words: Redox Biology, Reactive Oxygen Species, Arrhythmia

Paeonol Induces Thermogenesis by Suppressing Endoplasmic Reticulum Stress via NRF2 Activation in Beige Adipocytes

Ja Yeon Park[1], Gahee Song, Wenjun Jiao, Se Jin Jung, Beomsu Kim, Sang Hee Kim, Jisoo Han, Taekyoung Kong, Jae-Young Um*

Kyung Hee University, Seoul, 02447, Republic of Korea.

**Correspondence email: wkdusaos5357@naver.com*

Abstract

Endoplasmic reticulum (ER) stress is closely associated with various metabolic diseases, such as obesity and diabetes. Although the relationship between ER stress and white adipocytes has been extensively studied, the role of ER stress in beige adipocyte differentiation remains largely unexplored. In this study, we investigated the effects of paeonol on beige adipocyte differentiation through the regulation of ER stress. Our findings demonstrate that paeonol promotes the browning of pre-adipocytes by increasing the expression of beige markers such as TBX1 and CD137, as well as thermogenesis factors including UCP1 and PGC1α in primary cultured brown adipocytes. Moreover, paeonol significantly inhibited ER stress markers such as CHOP and GRP78, suggesting that paeonol activates beige adipocyte differentiation by regulating ER stress. Additionally, to verify the mechanism by which paeonol regulates ER stress, we assessed ROS levels, a representative inducer of ER stress, using DCFDA staining. Paeonol dose-dependently suppresses ROS levels, and this ROS inhibition was attributed to the activation of NRF2, a crucial regulator of ROS. Consequently, our results demonstrate that paeonol enhances beige adipocyte differentiation by regulating ER stress through NRF2 activation, indicating that paeonol may serve as a potential therapeutic agent for obesity.

Key Words: Beige Differentiation, ER Stress, Reactive Oxygen Species, NRF2, Obesity, Redox Biology

Suppression of O-GlcNAc transferase (OGT) inhibits adipogenesis in 3T3-L1 adipocytes through the modulation of PPAR γ O-GlcNAcylation

Hoang Hai Ngo[1] and Young-Sam Keum[*]

[1] *College of Pharmacy and Integrated Research Institute for Drug Development, Dongguk University, 32 Dongguk-ro, Goyang, Gyeonggi-do 10326, Korea*

**Correspondence email: haingo240194@gmail.com*

Abstract

The post-translational modifications (PTMs) play an important role in the control of the protein function. The O-linked N-acetylglucosamine (O-GlcNAc) modification is a type of nutrient-sensitive PTM and occurs at serine or threonine residues by a single pair of enzymes, O-GlcNAc transferase (OGT) and O-GlcNAcase (OGA). Aberrations in protein O-GlcNAcylation and OGT have been associated with a range of human diseases, such as obesity, diabetes mellitus, and cancer. In another context, the levels of O-GlcNAc proteins within the cellular milieu demonstrate a complex interrelationship with the availability of nutrients. In the present study, we have observed that serum deprivation activates AMP-activated kinase (AMPK) to phosphorylate OGT at Thr444, resulting in the proteolysis of OGT by CUL1/SKP2 E3 ubiquitin ligase. Through immunoprecipitation methods, we observed the involvement of OGT in the O-GlcNAcylation of peroxisome proliferator-activated receptor γ (PPARγ), a master regulator of adipogenesis and lipid storage. Furthermore, the treatment of AICAR (an AMPK activator), OSMI-1 (an OGT inhibitor), or silencing of OGT led to the suppression of 3T3-L1 cell differentiation. Finally, we provide evidence that suppression of OGT levels coincided with a reduction in lipid synthesis during serum deprivation *ex vivo* and *in vivo*. Together, our results show the inhibition of O-GlcNAc transferase (OGT) attenuates adipogenesis via the modulation of PPARγ O-GlcNAcylation.

Key Words: O-GlcNAc transferase (OGT), CUL1/SKP2 E3 ubiquitin ligase, Peroxisome proliferator-activated receptor γ (PPARγ), adipogenesis.

YY1 nitration participates in T2DM induced-cardiomyocyte lipotoxicity by inhibiting Anxa3 transcription

Jiayin Chai[1]（柴嘉音）, Wen Wang[1]

Affiliation: Department of Physiology and Pathophysiology, School of Basic Medical Sciences, Capital Medical University, Beijing, China

**Correspondence email: 1544387796@qq.com*

Abstract

Diabetes cardiomyopathy (DbCM) is one of the most serious complications of diabetes.Dyslipidemia in Type II diabetes (T2DM) patients will cause the accumulation of lipid droplets in myocardialcytes and induce severe lipotoxicity, which is considered to be one of the important reasons for DbCM. This study is aimed to explore the potential molecular mechanism of myocardial lipid deposition induced by T2DM at the level of protein post-translational modification. It has been confirmed that in myocardial tissue of T2DM ANXA3 plays an important role in maintaining myocardial homeostasis by regulating the microlipophagy and autophagy of myocardialcytes. It's well known that the nitrosative stress level is elevated in DbCM, leading to an abnormal increase in protein nitration. The nitrative modification of YY1which is the transcription factor of *Anxa3*, increased, led to a decrease in its transcription ability for *Anxa3*, resulting in lipid deposition and damage to myocardialcytes. Overall, this study suggests that anti-YY1 nitration and enhanced ANXA3 mediated microlipophagy and autophagy may be a promising target in the prevention and treatment of lipid toxicity in DbCM.

Key Words: T2DM, natrition, lipophagy, lipid desposition, lipotoxicity

α -Ketoglutarate pretreatment prevents hyperlipidemia-induced endothelial injury and fatty liver by ameliorating mitochondrial dysfunction and oxidative stress

Danyu Cheng[1]（程丹雨）, Jiankang Liu[1, 2*]

[1]*Center for Mitochondrial Biology and Medicine, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, and First Affiliated Hospital Xi'an Jiaotong University, Xi'an, Shaanxi 710049, China.*

[2]*School of Health and Life Sciences, University of Health and Rehabilitation Sciences, Qingdao, Shandong 266071, China*

**Correspondence email: danyucheng9643@163.com; j.liu@mail.xjtu.edu.cn*

Abstract

Hyperlipidemia is a common human disease characterized by high blood lipids and associated with an increased risk of a series of metabolism-related diseases, such as atherosclerosis and non-alcoholic fatty liver disease. How to prevent dyslipidemia safely and effectively so as to alleviate hyperlipidemia and its complications has been a hot topic in academic research. α-Ketoglutarate (AKG), a crucial intermediate in the tricarboxylic acid cycle that connects amino acid metabolism and glucose oxidation processes, has been demonstrated to regulate various cellular activities including energy metabolic processes. Recent studies have found that plasma AKG levels are negatively correlated with BMI, suggesting a correlation between AKG and metabolic syndrome. However, the role of AKG in hyperlipidemia and its induced endothelial and hepatic injuries are still unclear. Our findings indicate that effectively protects hyperlipidemia-induced endothelial injury and fatty liver by ameliorating mitochondrial dysfunction and oxidative stress. Mechanistic studies suggest that AKG regulated mitochondrial function and redox homeostasis through the PGC-1α/Nrf2 pathway. In summary, our results reveal the role of AKG in ameliorating hyperlipidemia-induced endothelial injury and fatty liver, suggesting a promising role of AKG as an endogenous mitochondrial nutrient in treating hyperlipidemia and its complications.

A fluorescence-enhanced near-infrared fluorescent probe for real-time imaging of protein sulfenic acids in oxidative stress

Zhixuan Feng [a]（冯芷璇）, Ping Li [a], Libo Du [a]

[a]*State Key Laboratory for Structural Chemistry of Unstable and Stable Species, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, PR China*

**Correspondence email: 18822133464@163.com*

Abstract

Protein sulfenic acids represent a crucial transient species in oxidative stress and an important post-translational modification that play a key role in oxidative signal transduction of many biological and pathological processes. Hence, the development of fluorescent probes to image protein sulfenic acids is of great significance for the study of redox homeostasis in living system. However, most of the fluorescence probes are “always on”, and their fluorescence signals remain “on” regardless of whether they are combined with the target. We herein report a novel near-infrared (NIR) fluorescent probe（HCA-CHD）distinguished by its fluorescence enhancement upon protein sulfenic acids interaction. HCA-CHD constructed with a hemicyanine dye as the signal unit and 1,3-cyclohexanedione as a sulfenic acid-reactive group. This probe could act as a promising fluorescent probe for specifically detecting sulfenic acids. Based on the good near-infrared imaging capabilities of the probe, which is employed to detect protein sulfenic acids in living cells and cancer mice. We hope that this fluorescence-enhanced NIR probe can become an effective tool to study the mechanism of protein sulfenic acids in physiological processes in vivo and offers guidance for research on sulfenic acid-related diseases.

Acute lung injury induced by acid aspiration or lipopolysaccharide leads to liver injury and hepatic regulated cell death in mice

Cheng Peng[1,2]（彭程）, Zhengpeng Zeng[1,2], Gang Yu[1,2], Yingbi Zhou[1], Bin Liu*[1,2]

[1]*Cardiovascular Research Center, Shantou University Medical College, Shantou, China*
[2]*Guangdong Provincial Key Laboratory of Infectious Diseases and Molecular Immunopathology, Shantou University Medical College, Shantou, China*
Shantou University Medical College, 22 Xin-Ling Rd, Shantou, 515041 China

**Correspondence email: 875082296@qq.com*

Abstract

BACKGROUND: Acute lung injury (ALI) and its severe form acute respiratory distress syndrome (ARDS) are life-threatening diseases, which are usually caused by severe infection, trauma or aspiration. Liver injury is common in ARDS patients, associated with poor prognosis of patients. Cell death is a specific manifestation of tissue injury and plays an important role in the occurrence and development of many diseases. However, the mechanism of how acute lung injury induces liver injury and liver cell death remains unclear.

METHODS: C57BL/6N mice were intratracheally instilled with HCl (0.1 N, 2 μl/g) or LPS (30 mg/kg) to establish ALI model. Mice were sacrificed after 12 hours. Blood samples were collected for determination of serum transaminase and total bilirubin levels. The histological damage of lung and liver were assessed, and the level of liver inflammation was reflected by the level of inflammatory factors and inflammatory cells infiltration. Markers of regulated cell death (RCD) were detected by western blotting.

RESULTS: Compared with the vehicle group, the pathological scores of lung tissue, the total protein concentration of bronchoalveolar lavage fluid (BALF) and serum transaminase levels were significant elevated in HCl- or LPS-induced ALI mice. But there was no significant difference in serum total bilirubin among the groups. Inflammatory indicators, including neutrophil infiltration level， TNF-α content and the expression of CXCL-1 mRNA, showed significant increases in liver tissue of ALI mice. The mRNA expression levels of MCP-1, TNF-α and IL-1β in the liver tissue were increased in LPS-treated mice only. Expressions of apoptosis-related markers reveled by Western blotting and the number of TUNEL-positive cells in liver tissue of ALI mice were increased. Only the LPS-treated mice had significant increases in necroptosis and the inflammasome marker proteins in liver tissue. Markers of Western blotting showed that ferroptosis not induced by the treatments.

CONCLUSIONS: LPS- or HCl aspiration-induced ALI causes liver regulated cell death and secondary liver injury in mice by increasing the level of liver inflammatory factors like TNF-α and neutrophil infiltration. However, the cell death pattern are different between the two groups, hepatocytes only show apoptosis in HCl group, but additionally undergo regulated necrosis in LPS-induced ALI.

Key words: Acute lung injury; Liver injury; Cell death; Inflammation; Neutrophils

COX7A1 heightens the susceptibility of human NSCLC cells to cystine deprivation-induced ferroptosis

Rongrong Liu （刘蓉蓉）, Yetong Feng, Mengjiao Shi, Pengfei Liu

National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University

**Correspondence email:727806615@qq.com*

Abstract

COX7A1, a subunit of cytochrome c oxidase, holds an important position in the super-assembly which integrates into multi-unit heteromeric complexes peripherally in the mitochondrial electron transport chain (ETC). Recently, some studies indicated the significant potential of COX7A1 in cancer metabolism and therapy. However, the underlying metabolic process and therapy mechanism remain unclear. In this study, COX7A1-overexpressed cell line was established via lentivirus transduction. The relationship between COX7A1 and ferroptosis, a novel form of cell death driven by iron-dependent lipid peroxidation, was further analyzed in different human non-small-cell lung carcinoma (NSCLC) cells respectively. Our results showed that COX7A1 increased the sensitivity of NSCLC cells to the ferroptosis induced by cysteine deprivation via enhancing the tricarboxylic acid (TCA) cycle and the activity of complex IV in mitochondrial ETC. Meanwhile, COX7A1 suppressed mitochondrial dynamics as well as mitochondrial biogenesis and mitophagy through blocking autophagic flux. The autophagy activator, rapamycin, relieved the autophagic blockage and further strengthened the sensitivity to cysteine deprivation-induced ferroptosis of NSCLC cells in vitro and in vivo. Taken together, our data indicate the close association of COX7A1 with cysteine deprivation-induced ferroptosis, and provide a novel insight into the therapy mode against human NSCLC.

Key Words: COX7A1, mitochondria, electron transport chain, tricarboxylic acid cycle, ferroptosis, non-small-cell lung carcinoma

Decomposable Nanodrugs Inducing Immunogenic Cell Death and cGAS-STING Pathway Activation for Enhanced Photodynamic Chemotherapy-Driven Immunotherapy

Chen-ChenLi（李晨晨）, Xu-YingLiu*, Yan-Fei Kang*

College of Laboratory Medicine, Hebei North University, 11 Diamond Street South, Zhangjiakou, 075000

**Correspondence email: kangyanfei172@163.com; liuxuying0045@163.com; 2242099379@qq.com*

Abstract

In this work, the DOX and photosensitizer Ce6 were encapsulated into a glutathione (GSH)/pH sensitive cinnamaldehyde dimers (CDC) to form nanodrug Ce6-DOX@CDC, leading to effectively induce ICD, activate STING pathway, and enhance the therapeutic effect. The nanodrug Ce6-DOX@CDC was decomposable within the tumor microenvironment (TME), and leaded to the release of DOX and Ce6. The released DOX and Ce6 not only killed tumor via damaging DNA and ROS production, but also induced prominent ICD and activate cGAS-STING pathway to improve the immunotherapy. In summary, it offer a promising method for enhancing the immunotherapy via inducing robust ICD and initiating the activation of the STING pathway.

Dehydrocostus lactone as a potential therapeutic agent for colorectal cancer and dextran sulfate sodium-induced colitis in mice

Sun-Young Hwang, Kwanhwan Wi, Young-Gwon Kim, and Mee-Hyun Lee*

College of Korean Medicine, Dongshin University, Naju, Jeonnam, 58245, Republic of Korea

**Correspondence email: tigger5368@naver.com*

Abstract

Purpose: This study aimed to evaluate the anticancer effects of dehydrocostus lactone (DCL) extracted from *Aucklandia costus* Falc. on colorectal cancer cell lines, as well as its anti-inflammatory effects in a dextran sulfate sodium (DSS)-induced colitis model. **Methods:** The toxicity of DCL was assessed on normal human dermal fibroblast (NHDF) cells, and its effects on cell viability were evaluated on HCT116 and HT29 colorectal cancer cell lines using the MTT assay. A soft agar assay was conducted to assess the inhibition of colony formation and growth. Flow cytometry was employed to analyze cell cycle distribution and apoptosis induction, while western blot analysis was performed to determine changes in the expression levels of proteins related to cell cycle regulation, apoptosis, and signaling pathway. For the *in vivo* study, female ICR mice were administered DSS in their drinking water to induce colitis, followed by treatment with DCL. The anti-inflammatory effects were evaluated by measuring changes in body weight, colon length, disease activity index (DAI). **Results:** DCL treatment exhibited no toxicity in NHDF cells while significantly reducing the viability of HCT116 and HT29 cells. DCL inhibited colony formation and growth in soft agar assays. Flow cytometry analysis demonstrated that DCL induced cell cycle arrest at the G2/M phase and increased apoptosis in colorectal cancer cells. Western blot analysis confirmed alterations in the expression of proteins involved in cell cycle arrest and apoptosis. Additionally, DCL inhibited the expression of phosphorylated AKT and its downstream signaling proteins. In the DSS-induced colitis model, DCL treatment significantly reduced weight loss, improved colon length, and lowered DAI scores. **Discussion:** DCL demonstrated potent anticancer effects on colorectal cancer cells by inhibiting cell viability, inducing G2/M phase cell cycle arrest, and promoting apoptosis, potentially through the inhibition of the AKT signaling pathway. Additionally, DCL effectively reduced inflammation in a DSS-induced colitis model. These findings suggest that DCL may serve as a therapeutic agent for the treatment of colorectal cancer and inflammatory bowel disease.

Key Words: Dehydrocostus lactone, Colon cancer, Dextran sulfate sodium, Colitis

Europium-modified carbon nitride nanosheets for smartphone-based fluorescence sensitive recognition of anthrax biomarker dipicolinic acid

Wenhao Du [a]（杜文浩）, Mi Yuan [b], Mingtai Sun[a,*], Chao Yuan[a,b,*], Suhua Wang[a,*]

[a] Guangdong Provincial Key Laboratory of Petrochemical Pollution Processes and Control, School of Environmental Science and Engineering, Guangdong University of Petrochemical Technology, Maoming 525000, People's Republic of China

[b] College of Biomedicine and Health, Huazhong Agricultural University, Wuhan 430070, People's Republic of China

Correspondence email: shifucha12500@gmail.com

Abstract

Humans can be infected with B. anthracis through indirect or direct contact with B. anthracis spores in soil, water, and meat, causing symptoms such as chest pain, fatigue, fever, and even shock. By detecting the biomarker 2, 6-pyridine dicarboxylic acid (DPA) produced by bacterial spores, the presence of Bacillus anthracis can be intuitively determined. Designing a set of efficient and sensitive detection methods is of great significance for maintaining public health and food safety. In this paper, we have successfully proposed an effective ratio fluorescence sensor, g-C_3N_4/CitNa/Eu^{3+}, for the detection of the unique biomarker of Bacillus anthracis -DPA. With the increase of DPA concentration, the emission intensity of g-C_3N_4 remained constant as a stable internal standard, while the fluorescence of Eu^{3+} was significantly enhanced due to the antenna effect. The linear range is 0.1 to 15μM, and the detection limit is 13nM. The g-C_3N_4/CitNa/Eu^{3+} probe sensor has the advantages of high sensitivity, good precision, good selectivity, high accuracy and simple preparation. In addition, the colorimetric fluorescence method developed shows relatively pronounced color changes that are easily recognized by the naked eye. Therefore, a portable test strip that does not require large expensive instruments and smart phone assisted bedside detection platform was developed for visual analysis of DPA, providing a powerful means for DPA analysis in the field and in resource-poor areas.

Exploring immune evasion mechanism mediated by superoxide anion of hepatic stellate cells by fluorescence imaging

Yuantao Mao[a]（毛元涛）, Xin Wang,[a]* Xia Li,[c]* Ping Li[a]*& Bo Tang[a,b]*

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.*

[b] *Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.*

[c] *Innovative Institute of Chinese Medicine and Pharmacy, Shandong University of Traditional Chinese Medicine, Jinan, China.*

**Correspondence email: lip@sdnu.edu.cn; lixia@sdutcm.edu.cn; xinwang@sdnu.edu.cn; tangb@sdnu.edu.cn*

Abstract

Whether and how the reactive oxygen species (ROS) generated by hepatic stellate cells (HSCs) promoting immune evasion of hepatocellular carcinoma (HCC) remains mysterious. Therefore, exploring the role of superoxide anion ($O_2^{\bullet-}$), the firstly generated ROS, in the immune evasion become necessary. In this work, we established a novel in situ imaging method for visualization of $O_2^{\bullet-}$ changes in HSCs based on a new two-photon fluorescence probe TPH. TPH comprises caffeic acid and HSCs targeting peptides. We observed that $O_2^{\bullet-}$ in HSCs gradually rosed during the activation, impairing the infiltration of $CD8^+$ T cells in HCC mice. Further studies reveal that the cyclin-dependent kinase 4 (CDK4) was deactivated by $O_2^{\bullet-}$, and then caused the up-regulation of PD-L1. Our work provides a detailed mechanism of aHSCs mediated immune evasion of HCC, which is expected to be potential targets for HCC immunotherapy.

Exploring Nitroproteomics in Cancer Biology: A Case Study of Early On set Gastric Cancer

Jae Won Oh[1], Su-Jung Kim[1], Kyu Jin Song[1], Eunju Kim[1], Kwang Pyo Kim[1,2†,]

1) Department of Applied Chemistry, Institute of Natural Science, Kyung Hee University, Yongin 17104, Rep ublic of Korea

2) Department of Biomedical Science and Technology, Kyung Hee Medical Science Research Institute, Kyun g Hee University, Seoul 02453, Republic of Korea

**Correspondence email: odinplate@naver.com*

Abstract

Nitration, a post-translational modification (PTM) that occurs under oxidative stress conditi ons, involves the formation of 3-nitrotyrosine through the interaction of nitric oxide synth ase (NOS) with reactive oxygen species (ROS) to produce peroxynitrite. Past studies in ni troproteomics have shown that nitrated proteins play significant roles in altered enzymatic functions, disruptions in cellular signaling and phosphorylation pathways, and protein deg radation. Despite its critical importance, the study of nitroproteomics and understanding th eir complex signaling mechanisms are still challenging due to the lower frequency of nitr ation compared to other PTMs such as phosphorylation and glycosylation. However, advan cements in mass spectrometry and the data from diverse studies have greatly enhanced ou r understanding of the nitroproteome. Using these technological advances, our study withi n the Early Onset Gastric Cancer (EOGC) project in the Clinical Proteomic Tumor Analy sis Consortium (CPTAC) revealed a strong link between protein nitration and key biologic al processes such as cell migration, inflammation, and actin polymerization in EOGC. Thi s study highlights the utility of advanced mass spectrometry and extensive proteomic data to elucidate the impact of nitration on cancer biology, emphasizing the link between nitr ation, MPO activity, and vital cellular processes in EOGC, which could lead to new thera peutic targets for intervention.

Hepatic Sinusoidal Endothelial Cells Targeted Delivery of Nitric Oxide via Glycosyl-modified Glycosidase to Treat Liver Fibrosis

Jingjie Tan（谭靖节）, Anqi Li, Yaru Chen, Jingli Hou*

Tianjin Medical University, Tianjin, 300070

**Correspondence email: lengyurui0615@163.com*

Abstract

Hepatic fibrosis is a common pathological process of chronic liver disease, leading to the development of cirrhosis. It is usually caused by activation of hepatic stellate cells (HSC) due to insufficient release of NO from hepatic sinusoidal endothelial cells (LSECs). As an endogenous gas signaling molecule, NO has great potential for the treatment of liver fibrosis and other liver diseases. LSECs is a key regulator of liver homeostasis, and targeted delivery of NO to LSECs may be useful in the treatment of liver fibrosis. Based on "bump and hole" strategy, an "engineered enzyme-NO prodrug" system was developed which can control release NO by engineered enzyme. Considering the abundant ManR on the surface of LSECs, we further modified the engineered enzyme by mannose to achieve LSECs-specific release NO by the affinity between mannose and ManR. Herein, a mannose-monomer sugar ligand M-IME and a three-antenna mannose-conjugate TM were designed and synthesized. Subsequently, the engineered enzymes were modified by the above ligands, and the obtained enzymes were characterized, such as catalytic activity, targeting property. Lastly, NO release from the modified enzyme and corresponding NO donor was detected by Griess reagent method. And NO targeting release was detected by Confocal assay in different cells (HSC, HepG2, LSECs, etc.).

Investigating the Relationship Between Tumor Stem Cells, Oxidative Stress, and Cisplatin Resistance in Ovarian Cancer

Jinzhi Lu [1,2,*]（鲁锦志）, Zewen Hu [2,3,†], Cunjian Yi [2,3]

[1] *Department of Laboratory Medicine, The First Affiliated Hospital of Yangtze University, Jingzhou 434000, China*

[2] *Hubei Provincial Clinical Research Center for Personalized Diagnosis and Treatment of Cancer, Jingzhou 434000, China*

[3] *Department of Obstetrics and Gynecology, The First Affiliated Hospital of Yangtze University, Jingzhou 434000, China; moon18390822196@yeah.net (D.L.); 2021710942@yangtzeu.edu.cn (Z.H.)*

**Correspondence email: jinzhilu2015@yeah.net (J.L.);*

Abstract

Objective: Cisplatin is an effective chemotherapeutic agent for ovarian cancer; however, resistance often leads to treatment failure. This study examines the relationship between cisplatin resistance, tumor stem cells, and oxidative stress, with a focus on reactive oxygen species (ROS). Methods: We established a tumor stem cell model using cisplatin-sensitive SKOV3 and resistant SKOV3-DDP human ovarian cancer cell lines. Cells were cultured in serum-free medium (SFM) with growth factors to enhance tumor sphere formation. We assessed the expression levels of stemness factors (SOX2, OCT4, NANOG) and markers (CD44, CD24, CD133, ALDH1) using RT-qPCR and Western blotting. Additionally, we employed small molecular compounds to modulate oxidative stress and gene editing techniques to further investigate ROS's role in cisplatin resistance. Results: SKOV3-DDP cells demonstrated accelerated tumor sphere formation compared to SKOV3 cells, indicating enhanced stem cell characteristics. Notably, mRNA levels of NANOG, OCT4, SOX2, and other markers were significantly elevated in SKOV3-DDP cells. Protein analysis revealed distinct profiles of stemness-related proteins, with increased oxidative stress markers in resistant cells. Conclusion: This study successfully enriched SKOV3-DDP tumor stem cells through serum-free culture and highlights their potential role in cisplatin resistance via oxidative stress mechanisms. Targeting these tumor stem cells by modulating ROS may improve therapeutic outcomes in ovarian cancer.

Key Words: Ovarian cancer, tumor stem cells, drug resistance, serum-free culture, Oxidative Stress.

Liposomes-encapsulated hERG Potassium Channel Probe for Glioblastoma Therapy and Imaging

Zhenzhen Liu,[a] Li Liu,[a]（刘丽） Tongtong Ban,[a] Ruihao Li, Xiao Zhang,[a] Wei Zhang,[a] Xin Wang,[a] Ping Li[a,c]*, and Bo Tang[a,b]*

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.*

[b] *Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.*

[c] *College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic China*

**Correspondence email: lip@sdnu.edu.cn; xinwang@sdnu.edu.cn; tangb@sdnu.edu.cn*

Abstract

Although hERG channel represents a promising target for cancer therapy or imaging, there are few works reported to explore its therapeutic potential because of possible cardiac toxicity. In this work, a novel near-infrared probe A8 for the oncogenic hERG channel is developed. This probe exhibits potent antitumor effect in glioblastoma cells, and then is encapsulated in a novel ApoE peptide modified pH-sensitive liposome to improve its efficiency across the blood-brain barrier and of tumor targeting. The obtained liposome ApoE-Lipo@A8 can significantly suppress the growth of the orthotopic glioblastoma xenografts with lower toxicity. Unbiased omics studies unveil some novel molecular mechanism underlying anti-tumor effect of hERG channel inhibition, including inhibiting the CDK2/4-pRB-E2F, PI3K-AKT-FOXM1, FA signaling pathway and triggering ER-stress dependent apoptosis and autophagy. Additionally, A8 is characterized with an aggregation-caused fluorescent quenching switch and can be used to lighting up hERG channel and further GBM imaging. This study systematically explores the therapeutic and imaging potential of hERG channel for glioblastoma, and provides a formulation method to address the challenges faced by hERG channel inhibitors in tumor treatment.

Manipulating disulfide bond formation of the Spike protein to inhibit the SARS-CoV-2 infection

Xinqian Li（李欣倩）, Ping Liu, Chih-chen Wang, Xi Wang, Lei Wang*

National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China,

**Correspondence email: wanglei@ibp.ac.cn.*

Abstract

The high mutation frequency of the spike (S) protein coding sequence in the SARS-CoV-2 genome facilitates immune evasion and challenges current therapeutics. However, the complex cysteine/disulfide pattern, involving 40 cysteine residues forming 15 disulfide bonds, is not only crucial for the structure and function of SARS-CoV-2 S protein but also remarkably conserved. Here we found that the folding and maturation of the S protein is a redox-sensitive process, strictly depending on endoplasmic reticulum sulfhydryl oxidase 1 alpha (Ero1α) and protein disulfide isomerase (PDI), the principal oxidative protein folding machines in eukaryotic cells. Treatment with reducing agent or mutation of cysteine residues in the S protein inhibits its processing by furin protease and plasma membrane localization. Mass spectrometric analysis indicates that disulfide bond formation in the S protein is not complete in *ERO1A* knockout HeLa cells. Knockout of either *ERO1A* or *PDI* of the HeLa cells decreases the oxidative folding rate of the receptor binding domain of the S protein. Ero1α depletion or treatment with Ero1α-PDI inhibitors blocks the plasma membrane localization of the S protein and significantly impairs its fusogenicity. Altogether, these findings reveal the molecular mechanism underlying the oxidative folding of the S protein in host cells and suggest that targeting this Achilles' heel could be a promising and broad-spectrum anti-coronavirus strategy.

Key Words: SARS-CoV-2, S protein, redox, Ero1α, PDI, disulfide bond

New approach to tumor therapy: Targeting the destruction of redox balance

ZHAO Sheng[1], Luo Qiwen[1]（罗其文）, MENG Yuzhou[1], CAI Wenxun[1], ZHANG Fuling[1], HUO Lingjie[1], SHI Dongyun[1,2]

[1]Key Laboratory of Metabolism and Molecular Medicine of the Ministry of Education, Department of Biochemistry and Molecular Biology, School of Basic Medical Sciences, Fudan University, Shanghai 200032, China.
[2]Free Radical Regulation and Application Research Center of Fudan University, Shanghai 200032, China.

**Correspondence email: dyshi@fudan.edu.cn*

Abstract

Redox balance plays a critical role in maintaining cellular health, including that of tumor cells, and an imbalance of which can lead to various forms of cell death.Tumor cells are characterized by a delicate balance between elevated oxidative stress and enhanced antioxidant capacity. This intricate equilibrium offers a unique perspective for cancer treatment by modulating reactive oxygen species (ROS) levels beyond cellular tolerability, thereby disrupting this balance. However, currently used chemotherapy drugs require larger doses to increase ROS levels beyond the redox homeostasis threshold, which may cause serious side effects. How to disrupt redox homeostasis in cancer cells more effectively remains a challenge. In this study, we found that sodium selenite and docosahexaenoic acid (DHA), a polyunsaturated fatty acid extracted from marine fish, synergistically induced cytotoxic effects in colorectal cancer (CRC) cells. Physiological doses of DHA simultaneously upregulated oxidation and antioxidant levels within the threshold range without affecting cell viability. However, it rendered the cells more susceptible to reaching the upper limit of the threshold of redox homeostasis, facilitating the elevation of ROS levels beyond the threshold by combining with low doses of sodium selenite, thereby disrupting redox homeostasis and inducing MAPK-mediated paraptosis. This study highlights the synergistic anticancer effects of sodium selenite and DHA, which induce paraptosis by disrupting redox homeostasis in tumor cells. These findings offer a novel strategy for more targeted and less toxic cancer therapies for colorectal cancer treatment. In the future, redox balance may serve as a crucial biomarker for personalized tumor therapy, which can be used for early warning, diagnosis, and treatment. Through dietary supplement, combined intervention and other treatment methods, tumor cells can be more accurately inhibited and normal cells protected. Therefore, redox balance regulation will become a new strategy for tackling and preventing tumor and ensuring health.

Key Words: reactive oxygen species; redox state; cell paraptosis; synergistic anticancer effects.

Repurposing Flubendazole for Glioblastoma Ferroptosis by Affecting xCT and TFRC Proteins

Wei Teng（滕炜）, Liangzhao Chu

Guizhou Medical University

**Correspondence email: t15564576971@163.com*

Abstract

New uses of old drugs hold great promise for clinical translation. Flubendazole is an FDA-approved antiparasitic drug that can target p53 and promote the apoptosis of glioblastoma (GBM) cells. But its damaging mechanism in GBM remains elusive. In this paper, we firstly explored the ferroptosis-inducing ability of Flubendazole on glioblastoma cells. After treating glioma cell lines U251 and LN229 with Flubendazole (DMSO < 1‰), their viabilities were concentration-dependently inhibited (LN229 IC50 = 0.5331 μM, U251 IC50 = 0.6809 μM) due to the induction of ferroptosis, which present MDA enhancement, ROS and lipid peroxides accumulation, mitochondrial membrane potential change and structure disorder. The ferroptosis-related proteins analysis revealed the upregulation of TFRC, DMT1 and p53 and the downregulation of xCT, FHC and GPX4 ($p < 0.05$). The all-atom docking of multiple proteins found that Flubendazole closely bound with xCT, TFRC, validating that Flubendazole could induce glioma ferroptosis via affecting xCT and TFRC proteins. Importantly, Flubendazole could damage the glioblastoma stem cells (GSC) that are highly resistant to other therapy, possessing advantaging in stopping glioma recurrence. This study delved into the glioma ferroptosis mechanism induced by Flubendazole, broadening its application and providing new ideas for new uses of other old drugs.

Key Words: Fubendazole, Ferroptosis, Glioblastoma, Glioblastoma stem cell

Respiratory exposure to lithium nickel manganese cobalt oxide particles induces multi-organ damage and disrupts redox homeostasis in mice

Junyi Wang（王君仪） Xin Fang Xianhang Yin Maojia Fu Changjun Hou Gang Wang Huihui Wang Jingbo Pi Yuanyuan Xu

China Medical University

**Correspondence email: 1910625901@qq.com*

Abstract

Objective: To assess the target organs and potential toxic mechanisms of respiratory exposure to lithium nickel manganese cobalt oxide ($LiNi_5Mn_3Co_2O_2$, NMC), a new cathode material in lithium batteries.

Methods: Thirty-six male C57BL/6J mice (8-12 weeks old) were randomly assigned to six groups (n = 6). NMC was administered via oropharyngeal aspiration either as a single exposure followed by 6 hours observation or as repeated exposures (25 or 100 mg/kg bw) for 3 days. Control groups received saline. Metal levels were quantified by ICP-MS. Organ damage was assessed using H&E and BALF cell counts. RT-qPCR was used to measure mRNA expression.

Results: A single NMC exposure led to rapid elevation in metal levels in blood, lungs, and kidneys within 6 hours. Repeated exposure significantly increased metal levels in the blood, lungs, livers, and kidneys ($P < 0.05$). Lung inflammation was evident, with increased leukocytes, neutrophils, and eosinophils in BALF ($P < 0.05$). The expression of *Ccl2, Cxcl1, Cxcr2, Il6,* and *Il1β* in lung tissue was significantly upregulated ($P < 0.05$). NRF2 downstream genes (*Nqo1, p62, Gclc, Hmox1*) were induced in key organs (lungs, livers, and kidneys) after a single exposure, with changes after repeated exposure: increased *Gclc* and *Hmox1* in lungs, reduced *Gclc* in liver, and elevated *Nqo1* in kidneys ($P < 0.05$).

Conclusion: Acute NMC exposure alters the lung immune environment, potentially causes kidney and liver damage, alongside significant disruption of redox homeostasis.

Acknowledgement: NSFC82241090.

Key Words: Lithium nickel manganese cobalt oxide, redox homeostasis, lung, liver, kidney.

Role and mechanism of nanomedicine with ROS regulating ability for differentiation therapy of myeloid neoplasia

Tao Wang[1]，Tao Wen[1]，Jie Meng [1]，Bing Han [2]，Haiyan Xu[1*]（许海燕）

1. Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

2. Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

**Correspondence email: xuhy@pumc.edu.cn*

Abstract

Differentiation therapy is an ideal alternative approach, which induces leukemia cells to differentiate towards a mature state, thereby detaching them from the malignant proliferative state and accelerating their apoptosis. Currently, only all-trans retinoic acid is clinically available for the differentiation therapy of acute promyelocytic leukemia. There is still an urgent need to develop differentiation-inducing drugs for other subtypes of acute myeloid leukemia. Reactive oxygen species (ROS) plays key roles in the maturation and differentiation of hematopoietic stem cells and hematologic tumor cells. Myeloid leukemia cells exhibit a distinct feature of redox imbalance and oxidative stress, and they also develop adaptive ROS homeostasis mechanisms. In response to these pathological characteristics, we comparatively studied the impact of prussian blue nanozymes, Au@Pt nanozymes, and hydrophilic realgar nanocrystals on ROS levels in myeloid leukemia cells and their abilities and mechanisms to induce multi-directional differentiation of leukemia cells. We also evaluated the therapeutic potential of Au@Pt nanozymes and hydrophilic realgar nanocrystals in a refractory acute myeloid leukemia mouse model. Results indicated that all three types of nanomaterials induced differentiation of leukemia cells by regulating intracellular ROS levels, with distinct characteristics in the direction of differentiation, and at the same time, demonstrating therapeutic effects on refractory leukemia. In summary, nanomedicines with ROS regulating ability are expected to play a role in the differentiation therapy of myeloid leukemia with redox imbalance.

Synthesis and study of β-glucuronidase controlled fluorescent probe

Anqi Li（李安琪）, Jingjie Tan, Yaru Chen and Jingli Hou*

Tianjin Medical University, Tianjin, 300070

**Correspondence email: 1146565819@qq.com*

Abstract

β-glucuronidase (β-GUS) is highly expressed in a variety of malignant tumors and participated in the process of tumor invasion and metastasis. Therefore, it can be used as a biomarker to detect cancerous tumors. Additionally, β-GUS levels are also significantly elevated in many physiological diseases. Therefore, it is of great significance to develop a small molecule fluorescent probe for real-time detectionof endogenous β-GUS. Herein, 7-hydroxy-9H-(1,3-dichloro-9,9-dimethylacridin-2-one) (DDAO), a near-infrared fluorescent core (600nm-650nm) was chosen as the report group. Two probes (βG-DDAO-1 and βG-DDAO-2) were synthesized by connecting DDAO and β-glucuronidyl together via a self-immolative linker. Subsequently, the following properties of the two probes were evaluated, such as responsiveness against β-GUS, sensitivity and dose response. Lastly, the probe was used to quantitatively detect β-GUS in various cancer cells and cancer tissues by confocal microscopy and in vivo imaging. Our work can shed a light on the relationship between β-GUS and cancer progress.

The acceleration of iron transport promotes the malignancy of glioma through Oxidizing 293 cysteine on sirt5 by the increased production of H2O2

Fei Wang （王飞）

Hebei Normal University

**Correspondence email: wangfei19980803@163.com*

Abstract

Iron plays a crucial role in promoting the proliferation of cancer cells. Deciphering the iron metabolism will provide new insights into the treatment strategies of glioblastoma (GBM). With the malignant transformation of glioma, the expression of transferrin receptor 1 (TfR1) and ferritin 1 (FPN1) increases. We detected cells overexpressing TfR1 and FPN1 in the areas of microvascular proliferation and palisade necrosis in GBM. To further investigate the effect of iron metabolism on malignant transformation of glioma, we constructed U251 overexpressing TfR1 and FPN1 (U251-SLC TfRC). U251-SLC TfRC exhibited an accelerated cell cycle and migration ability while increasing H_2O_2 production. Cysteine 293 on Sirt5 respond to the H_2O_2 signal to upregulate SMARCA4, thereby increasing the expression of CyclinD1 to accelerate cell cycle. We further revealed the mechanism of increased H_2O_2 in U251-SLC-TfRC: simultaneous overexpression of TfR1 and FPN1 accelerates iron transport, thereby promoting the synthesis of iron sulfur clusters to facilitate mitochondrial metabolism and the production of metabolic byproduct H_2O_2. In vivo results indicate that treatment with H_2O_2 scavengers has a good prognosis.

Key Words: GBM ,H_2O_2

β-Lapachone Enhances NETosis through Reactive Oxygen Species Generation: Mechanistic Insight in Neutrophil-Mediated Innate Immunity

Jisoo Han, Gahee Song, Wenjun Jiao, Ja Yeon Park, Se Jin Jung, Beomsu Kim, Sang Hee Kim, Taekyoung Kong, Hyun Jeong Kwak, Jae-Young Um

Kyung Hee University, Seoul 02447, Republic of Korea

**Correspondence email: jshan1998@gmail.com*

Abstract

Neutrophils play a crucial role in innate immune response by releasing neutrophil extracellular traps (NETs) as a defense mechanism against pathogen infection. During this process, neutrophils also generate reactive oxygen species (ROS), which are critical for both directly killing pathogens and inducing NETosis. β-Lapachone (βL) is a natural compound known to enhance ROS production, causing DNA damage and leading to pathogen killing. However, in neutrophil-mediated immune responses, the precise mechanism by which BL influences NETosis and its association with ROS production largely unknown. This study investigates whether βL induces NETosis by significantly increasing ROS production in bone marrow-derived neutrophils (BMDN) and differentiated HL-60 (dHL-60) cells. βL treatment was increased expression of NET formation markers including PAD4, gasdermin D, caspase-8, and MPO in BMDN and dHL-60 cells. We also observed that treatment with βL led to an increase in ROS production, accompanied by the upregulation of p-PKC α/β II, JNK, and AKT in both BMDN and dHL-60 cells. When these signaling pathways were inhibited, βL failed to upregulate ROS levels. Particularly, the JNK inhibitor SP600125 suppressed ROS to the lowest levels observed. Overall, this study provides comprehensive insights into BL as a novel pharmacological agent that influences neutrophil related to innate immune response by elucidating the mechanism of NETosis driven by BL-induced ROS production.

Key Words: β-lapachone, NETosis, Reactive oxygen species, Redox Biology

A Versatile Fluorescent Probe for Hydrogen Peroxide in Serotonergic Neurons of Living Mouse Brains with Depression

Feida Che [‡a]（车飞达）, Xiaoming Zhao[‡a], Qi Ding[a], Xiwei Li[a], Wen Zhang[a], Ping Li*[a, c], Xin Wang*[a], Bo Tang[a, b]

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.*

[b] *Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.*

[c] *College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic China*

**Correspondence email: lip@sdnu.edu.cn; xinwang@sdnu.edu.cn; tangb@sdnu.edu.cn*

Abstract

Depression, a prevalent mental illness, is intricately linked with the neurotransmitters in the brain, while serotonin as a crucial regulator of mood, energy levels, and memory, has been implicated in depression. So, the release of serotonin by serotonergic neurons plays a significant role in the development of depression. Notably, the foremost marker of oxidative stress hydrogen peroxide (H_2O_2), can interfere with the functioning of serotonergic neurons and potentially contribute to depression. Investigating the impact of H_2O_2 on serotonergic neurons could offer valuable insights into the mechanisms underlying depression. However, there are no effective tools for selectively imaging H_2O_2 in these neurons so far. To address this gap, we created a small molecular fluorescent probe, PF-H_2O_2, designed specifically for imaging H_2O_2 in serotonergic neurons under oxidative stress. PF-H_2O_2 exerts excellent serotonergic neurons-targetable and glorious selectivity for H_2O_2. Furthermore, we discovered increased H_2O_2 in serotonergic neurons of mice with depressive symptoms. Altogether, this endeavour unveils a pioneering tool for exploring pathophysiology linked to serotonergic neuronal dysfunctions.

DDAH1 attenuates MPTP-induced Parkinson's disease impairment via FOXO3 mediated signals

Zhirui Li [a,b#]（李祉睿）, Yixuan Li [a#], Fuyao Xiao [a#], Yuming Zhao [a*]

[a] *Department of Pharmacology, School of Basic Medical Sciences, Capital Medical University, Beijing，100069, P.R. China(*Corresponding Author)*

[b] *Beijing Tongren Hospital affiliated to Capital Medical University, Capital Medical University, Beijing，100069, P.R. China*

**Correspondence email: 2014016@mail.ccmu.edu.cn; yumingzhao@ccmu.edu.cn*

Abstract

Forkhead box protein O3 (FOXO3), a transcription factor that promotes cellular antioxidant defense as an imperative regulator of cellular stress response, plays an important protective role in Parkinson's disease (PD). However, the related mechanism by which endogenous anti-oxidative defense system protects against PD still remains elusive. Dimethylarginine dimethylamine hydrolase 1(DDAH1), as a response factor, might be a protective player in various diseases. We hypothesized that it could alleviate dopaminergic neuronal damage caused by PD by modulating the transcription of the FOXO3 gene, which is involved in antioxidant defense as well as autophagy after PD injury. After the 1-methyl-4-phenyl-1,2,3,6-tetrahydro pyridine (MPTP) treatment, the expression of DDAH1 in the midbrain was significantly increased. By comparing the results among DDAH1 transgenic mice, DDAH1 general knockout mice, and C57bl/6N wild-type mice, we discovered that DDAH1 could reverse MPTP-induced dopaminergic neuron loss, rescue substantia nigra neuron damage, and ameliorate further motor deficits that may be associated with the down-regulation of FOXO3 phosphorylation levels in the midbrain, which in turn inhibited the occurrence of oxidative stress and regulated aberrant autophagy.

Discovery of potent LRRK2 inhibitors by ensemble virtual screening strategy and bioactivity evaluation

Xiaoqing Gong [1], Shuli Li [1]（李淑黎）, Junli Huang [1], Shuoyan Tan, Qianqian Zhang, Yanan Tian, Qin Li, Lingling Wang, Henry H.Y. Tong, Xiaojun Yao, Chunxia Chen [*], Simon Ming-Yuen Lee [*]and Huanxiang Liu [*]

State Key Laboratory of Quality Research in Chinese Medicine and Institute of Chinese Medical Sciences, University of Macau, Macao, China. 999078,

**Correspondence email: yc27521@um.edu.mo*

Abstract

Leucine-rich repeat kinase 2 (LRRK2) has been reported to be associated with familial and idiopathic Parkinson's disease (PD) risk and is a promising target for drug discovery against PD. To identify novel and effective LRRK2 inhibitors, an ensemble virtual screening strategy by combining fingerprint similarity, complex-based pharmacophore and structure-based molecular docking was proposed and applied. Using this strategy, we finally selected 25 compounds from ~1.7 million compounds for in vitro and in vivo tests. Firstly, the kinase inhibitory activity tests of compounds based on ADP-Glo assay identified three most potent compounds LY2023-19, LY2023-24 and LY2023-25 with IC_{50} of 556.4 nM, 218.1 nM and 22.4 nM for LRRK2 G2019S mutant, respectively. The further cellular experiments also indicated that three hit compounds significantly inhibited Ser935 phosphorylation of both wide-type and G2019S LRRK2 with IC_{50} ranging from 27 nM to 1674 nM in HEK293T cells. The MD simulations of three compounds and G2019S LRRK2 showed the hydrogen bond formed by Glu1948 and Ala1950 is crucial for the binding of LRRK2. Afterwards, 6-OHDA-induced PD zebrafish model was constructed to evaluate the neuroprotective effects of hit compounds. The locomotion of the 6-OHDA treated zebrafish larvae was improved after treatment with LY2023-24. The obtained results can provide valuable guidance for the development of PD drugs by targeting LRRK2.

'Environmental standard limit concentration' arsenic exposure is associated with anxiety, depression, and autism-like changes in early-life stage zebrafish

Yuanhui Zhu（朱原慧）, Yan An

Department of Toxicology, School of Public Health, Jiangsu Key Laboratory of Preventive and Translational Medicine for Geriatric Diseases, MOE Key Laboratory of Geriatric Diseases and Immunology, Suzhou Medical College of Soochow University, Suzhou, Jiangsu 215123, P.R. China.

**Correspondence email: zbzyhcom@163.com*

Abstract

Arsenic is a worldwide environmental pollutant that can impair human health. Previous studies have identified mental disorders induced by arsenic, but the environmental exposure concentrations in the early life stages associated with these disorders are poorly understood. In the present study, early-life stage zebrafish were used to explore the effects on mental disorders under 'environmental standard limit concentrations' arsenic exposures of 5, 10, 50, 150, and 500 μg/L. The results showed that arsenic exposure at these concentrations changed the locomotor behavior in larval zebrafish and was further associated with anxiety, depression, and autism-like behavior in both larval and juvenile zebrafish. Changes were noted at benchmark dose limit (BMDL) concentrations as low as 0.81 μg/L. Transcriptomics showed that immediate early genes (IEGs) fosab, egr1, egr2a, ier2b, egr3, and jund were decreased after arsenic exposure in larval and juvenile zebrafish. Nervous system impairment and anxiety, depression, and autism-like behaviors in early-life stage zebrafish at 'environmental standard limit concentrations' may be attributed to the downregulation of IEGs. These findings in zebrafish provided new experimental support for an arsenic toxicity threshold for mental disorders, and they suggest that low levels of environmental chemicals may be causative developmental factors for mental disorders.

Key Words: Arsenic, early-life stage zebrafish, mental disorders, 'environmental standard limit concentration', Bayesian Benchmark Dose.

Exploring the Neuroinflammatory Pathways of 8-oxoGTP and Their Effects on Cognitive Decline

Jin Li[1]（李瑾）, Jia-Xin Pan[1], Rui Li[1], Zi-Hui Wang[1], Xu-Fan Gao[1], Jian-Ping Cai[1]

[1] *The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital/National Center of Gerontology of National Health Commission, Beijing, China, 100730.*

**Correspondence email: niyani88@126.com; caijp61@vip.sina.com*

Abstract

Neuroinflammation mediated by continuously activated glial cells may play a core role in neurodegenerative processes and cognitive deficits. Oxidative stress (OS) is considered to be one of the main underlying mechanisms of neurodegenerative diseases and is closely related to other pathological events. The cytoplasmic 8-oxoGTP generated by GTP oxidation increased during OS. On the one hand, 8-oxoGTP can serve as a substrate for RNA synthesis and cause RNA oxidation, leading to impaired protein synthesis, on the other hand, it can be used as a small molecule to regulate signaling. Given the susceptibility of 8-oxoGTP, free 8-oxoGTP as a signaling modulator requires more in-depth study. In this study, we administered multiple intracerebroventricular injections of 8-oxoGTP to SAMP8 mice and observed a significantly impaired performance in cognitive in behavioral experiments. Immunohistochemical analysis further demonstrated a marked reduction in the number of neurons in the cortical and hippocampal regions, accompanied by a significant increase in the number of activated microglia and elevated secretion of inflammatory cytokines. Cellular experiments indicated that 8-oxoGTP activates microglia by triggering the MAPK, AKT, and NF-κB signaling pathways, promoting an inflammatory phenotype. This mechanism highlights the critical role of microglia in 8-oxoGTP-induced neuroinflammation. Our study reveals the significant impact of 8-oxoGTP on neuroinflammation and cognitive decline, providing a theoretical foundation for exploring related therapeutic strategies.

Functional study of TMPRSS6 in APP/PS1 mouse

Sun Hongtao（孙洪涛）

College of Life Sciences, Hebei Normal University, Shijiazhuang 050024, Hebei Province, China

**Correspondence email: 2130049171@qq.com*

Abstract

Iron overload in the brain and iron-induced oxidative damage have been considered to play key roles in the pathogenesis of Alzheimer's disease (AD). In recent years, a large number of studies have shown that oxidative stress was participated in the pathological process of AD, including disorders of metal ion metabolism, especially iron metabolism. Iron is a major source for generating highly toxic reactive oxygen species (ROS), which extensively deposits in the brain of patients with neurodegenerative diseases, primarily responsible for the pathogenesis of several neurological disorders. In the brains of AD patients, Aβ has high affinity for iron, which accelerates its accumulation. Moreover, the localization of iron in brain plaques enhances the formation of H_2O_2 and oxidative stress, resulting in neurotoxicity in AD brain. The type II transmembrane serine protease (TTSP) family is a class of proteolytic enzymes that are fixed to the cell membrane through the transmembrane region of the amino terminus. Tmprss6 is one of these and plays a key role in iron homeostasis by modulating hepcidin, a hepatic peptide hormone that binds to and downregulates ferroportin 1 (FPN1), the only known cellular iron transporter. The Alzdata database (http://www.alzdata.org), which collected a large amount of data on Alzheimer's disease, showed a significant increase in Tmprss6 in the hippocampus, which was experimentally demonstrated in APP/PS1 mice. Injecting a neuron-specific promoter of AAV virus into the hippocampus of APP/PS1 mice to knock down Tmprss6 not only allowed iron to be excreted from neurons via FPN1, but also reduced Aβ levels in the brain. Eventually, the iron overload in the brain was improved, and ACSL4 levels in the hippocampus were significantly reduced, while GPX4 levels also increased, which in turn reduced ROS levels in the brain. Knocking down Tmprss6 mitigated neuronal damage by reducing oxidative stress levels in the brain and delayed the progression of AD.

GSNOR, a new player in depression

Chuanxin Sun[1]（孙传鑫）, Xinhua Qiao[1] and Chang Chen[1,2*]

[1] *Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China*

[2] *University of Chinese Academy of Sciences, Beijing 100049, R China*

**Correspondence email: changchen@ibp.ac.cn*

Abstract

Depressive disorder has become a serious medical and social problem due to its high prevalence, high recurrence rate, high burden, high disability rate and high suicide rate. Numerous studies have demonstrated that nitric oxide (NO) plays a crucial role in the development and progression of depression Investigating the specific mechanisms by which the NO signaling pathway influences depression has become a new research direction in the treatment of this disorder. Our finds indicate that S-nitrosoglutathione reductase (GSNOR), the key enzyme that metabolizes intracellular nitric oxide (NO) and regulates S-nitrosation, was significantly decreased in the hippocampus of a chronic unpredictable mild stress (CUMS) mouse model. This result suggests that GSNOR plays a significant role in depression. Further behavioral assessments, including the forced swim test, tail suspension test, and open field test, revealed that GSNOR knockout mice displayed an increased susceptibility to depression-related phenotypes induced by CUMS. We further developed a Nestin Cre-conditional GSNOR overexpression mouse model. Notably, overexpression of GSNOR in neurons alleviated CUMS-induced depression-related behaviors in these mice. Based on this original discovery, our mechanistic investigation focused on the effects of GSNOR on the synthesis, transport, reuptake, and metabolism of neurotransmitters associated with depression. Analysis of S-nitrosation modification using quantitative proteomics revealed decreased S-nitrosation of gamma-aminobutyric acid transporter-1 (GAT1) in GSNOR knockout mice. In summary, our research identifies GSNOR as a novel factor in depression, suggesting that further study of GSNOR could provide theoretical insights into the susceptibility, onset, and progression of depression.

Key Words: S-nitrosation modification; S-nitrosoglutathione reductase; depression; Nitric oxide

Hydrogen Peroxide in Midbrain Sleep Neurons Regulates Sleep Homeostasis

Yujing Tian（田玉静）, Luwei Kang, Danqian Liu

Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences, Shanghai 200031, China

**Correspondence email: yjtian@ion.ac.cn*

Abstract

Sleep could protect animals from oxidative damage, yet the dynamic interplay between the brain redox state and sleep regulation remains unclear. Here we show that acute sleep deprivation in mice caused a general increase in brain oxidation level, particularly in sleep regulating brain regions. Real-time in vivo imaging of intracellular hydrogen peroxide (H_2O_2) dynamics revealed that in nigra sleep neurons, the increase in cytosolic but not mitochondrial H_2O_2 reflected sleep pressure by positively correlating with the duration of wakefulness. By controllable manipulation of intra-neuronal H_2O_2 using chemogenetic and optogenetic approaches, we discovered that physiological low-level H_2O_2 elevation significantly enhanced sleep initiation, in a manner dependent on TRPM2 (transient receptor potential melastatin 2) channel, although excessive H_2O_2 caused brain inflammation and sleep fragmentation. Together, our study demonstrates intraneuronal H_2O_2 as an important signaling molecule that translates brain redox imbalance into sleep drive, and underscores the significance of oxidative eustress in midbrain sleep neurons for sleep regulation

Improving mitochondrial function with arachidonic acid supplementation to alleviate cognitive deficits in schizophrenia patients

Yan GAO（高琰）, Xiaowen HU*, Chunling WAN*

Bio-X Institutes, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders (Ministry of Education), Shanghai Jiao Tong University, Shanghai 200030, China

**Correspondence email: gao_yan@sjtu.edu.cn; xiaowen@sjtu.edu.cn; clwan@sjtu.edu.cn.*

Abstract

Objective: Mitochondrial dysfunction was recognized as one of pivotal contributors to schizophrenia associated with cognitive impairment. Potential of arachidonic acid to improve cognitive levels in schizophrenia has been reported, however, the underlying mechanisms remain unclear.

Methods: Here we investigate the mitochondrial lipid profile by lipidomic based on Liquid Chromatography-Mass Spectrometry (LC-MS) and cognitive performance by the Cambridge Neuropsychological Test Automated Battery® (CANTAB®) system. The Weighted Gene Co-expression Network Analysis (WGCNA) was performed to elucidate the correlation between lipid profile and cognitive performance.

Furthermore, an adjunctive intervention involving arachidonic acid (AA) supplementation (338 mg/day) was implemented in schizophrenia for six weeks. The primary outcome was cognitive performance. To investigate the underlying mechanisms of the observed improvements, comprehensive mitochondrial lipidomic and transcriptomic analyses were conducted.

Results: Our results indicated a highly disturbed mitochondrial lipid profile attributed to the abnormal oxidative stress in schizophrenia patients, with a higher level of oxidative pressure correlating with more severe cognitive impairment.

Following a six-week supplementation with AA in schizophrenia patients, cognitive deficits were alleviated, the oxidative lipids levels were reduced, mitophagy to clear dysfunctional mitochondria was activated, and ROS-induced ferroptosis was suppressed. Additionally, the improvements in cognitive levels, particularly in reaction latency and memory accuracy, were associated with reduced oxidative stress.

Conclusion: The implications of our findings suggest that mitochondrial dysfunction may serve as a potential therapeutic target for cognitive impairments in schizophrenia. This insight suggests a promising direction for further research and the development of nutritional strategies, which may have implications for both the prevention and treatment of cognitive deficits.

Key Words: Mitochondria; arachidonic acid; cognition; schizophrenia; oxidative stress; ferroptosis

Melatonin derivative 6a protects Caenorhabditis elegans from formaldehyde neurotoxicity via ADH5

Mengting Chen[1], Zijie Wu[1], Xinjie Zhang[1], Na Feng[1,*]（冯娜）

[1]*School of Pharmacy and Food Engineering, Wuyi university, Jiangmen 529030, China*

**Correspondence email: wyuchemfn@126.com*

Abstract

Formaldehyde (FA) is a carcinogen that is not only widespread in the environment, but is also produced endogenously by metabolic processes. In organisms, FA is converted to formic acid in a glutathione (GSH)-dependent manner by alcohol dehydrogenase 5 (ADH5). The abnormal accumulation of FA in the body can cause a variety of diseases, especially cognitive impairment leading to Alzheimer's disease (AD).

In this study, melatonin derivative 6a (MD6a) markedly improved the survival and chemotactic performance of wild-type *Caenorhabditis elegans* exposed to high concentrations of FA. MD6a lowered FA levels in the nematodes by enhancing the release of covalently-bound GSH from S-hydroxymethyl-GSH in an *adh-5*-dependent manner. In addition, MD6a protected against mitochondrial dysfunction and cognitive impairment in beta-amyloid protein (Aβ) transgenic nematodes by lowering endogenous FA levels and reducing Aβ aggregation in an *adh-5*-dependent manner. These results suggest that MD6a detoxifies FA via ADH5 and protects against Aβ toxicity by reducing endogenous FA levels in the *C. elegans* AD models.

In summary, we revealed the pharmacological mechanism of MD6a against FA neurotoxicity, which catabolizes FA through ADH5 to release GSH, thereby mitigating exogenous FA damage and reducing endogenous FA in AD. Our findings strongly suggest that ADH5 would be a pivotal therapeutic target for the prevention and effective management of FA toxicity, as well as for the alleviation of AD.

Key Words: Formaldehyde; Alzheimer's disease; Melatonin derivative; ADH5; GSH

nos2b regulates injury-induced cxcl18b-defined transitional state Müller Glia proliferation in the zebrafish retina

Aojun Ye[1,2]（叶傲君）, Jie He[2,3*], Chang Chen[1,2*]

[1]*Key Laboratory of Biomacromolecules (CAS), National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China.*
[2]*University of Chinese Academy of Sciences, Beijing 100049, China.*
[3]*State Key Laboratory of Neuroscience, CAS Center for Excellence in Brain Science and Intelligence Technology, Institute of Neuroscience, Chinese Academy of Sciences, Shanghai 200031, China.*

**Correspondence email: yeaojun17@mails.ucas.ac.cn*

Abstract

Zebrafish quiescent Müller glia (MG) can respond to the retina injury by re-entering the cell cycle, a critical step evolutionarily absent from their mammalian counterpart, which is essential for neuron regeneration program. MG could regenerate all retinal fates after the injury in the zebrafish retina by undergoing reprogramming and produced MG derived progenitors. However, the molecular and cellular mechanism driving this species-specific injury-induced MG proliferation may shed the light on new therapeutic strategy to repair human retina diseases but remains largely understood. In our study, single-cell transcriptome analysis reveals the landscape of injury-induced MG state progression from the quiescence to proliferation. We identified the injury-induced MG proliferation via cxcl18b-defined the transitional states. Notably, the cxcl18b-defined MG transitional states recapitulate molecular features of retinal developmental programs. Additionally, we discovered that nos2b is crucial for MG entry into the proliferation via nitric oxides signaling. Cell-specific knockout of nos2b in cxcl18b+ MG significantly reduced the MG proliferation after injury. In conclusion, our findings revealed the novel molecular and cellular mechanisms underlying the transition of MG from quiescence to proliferation after the cone ablation in the zebrafish retina.

Overexpressed of ferrous iron ions triggers Neutrophil extracellular trap formation and contributes to multiple sclerosis

Shenyu Yan （颜深玉）

The University of Hong Kong

**Correspondence email: 454076575@qq.com*

Abstract

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease that afflicts approximately 2.8 million people worldwide. Iron-mediated oxidative stress plays critical role in neuronal damage and mediates neuroinflammation, but underlying mechanisms remain largely unknown. Iron homeostasis could maintain normal neurological function in central nervous system, because iron involved in the oxidative metabolism and the synthesis of neurotransmitters and myelin. Herein, by using experimental autoimmune encephalomyelitis (EAE) animal model, we tested the hypothesis that ferrous iron overload could be correlated with EAE pathogenic progress through migration from peripheral to central nervous system and induction of neutrophil leukocyte infiltration and neutrophil extracellular trap(NET) formation in both peripheral immune system and central nervous system. We found that ferrous iron-triggered NET formation in vitro and induced neuronal cell death by reactive oxygen species production. Neutrophils carried iron enter into central nervous system and induced oxidative stress, subsequently initiating ferroptosis and induced demyelination in the EAE pathogenesis. Therefore , we conclude that overload iron contributes to the and NET-induced ferroptosis led demyelination and inflammation during multiple sclerosis pathogenesis. Targeting this pathogenesis could be a novel therapeutic strategy to attenuate multiple sclerosis pathogenesis.

Key Words: ferroptosis, multiple sclerosis, neutrophil extracellular trap

Oxidative stress increased β-galactosidase activity in the brains of mice with depression

Deqiang Li[1]（李德强） Xin Wang[1] Ping Li[1,3] Bo Tang[1,2]

1.College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.

2.Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.

3.College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic China

**Correspondence email:2283688210@qq.com*

Abstract

Depression is a mental illness with high morbidity and mortality, closely related to oxidative stress in the brain. β-Galactosidase (β-Gal) is a key enzyme that regulates glycoprotein and glycolipid metabolism in biological systems. Under oxidative stress, the activity of β-Gal affects brain sugar metabolism, leading to disorders in brain function and triggering brain diseases such as depression. Therefore, revealing the changes in β-Gal activity and its related molecular mechanisms during the development of depression is crucial to understanding the pathogenic mechanisms of depression. However, there was currently a lack of imaging tools to monitor β-Gal activity in situ. Hence, we developed a fluorescent probe Gal-HCAF based on chalcone derivatives for real-time, in situ monitoring of β-Gal activity fluctuations in the brains of depressed mice. The D-galactoside glycosidic bond in the probe was specifically cleaved by β-Gal to release HCAF, which was enhanced fluorescence by ESIPT. In addition, the lipophilicity of Gal-HCAF was increased by introducing F atom, making it easier to cross the blood-brain barrier. Using Gal-HCAF, we successfully observed that β-Gal activity in PC12 cells increased significantly under oxidative stress. The results of in vivo imaging revealed for the first time that the activity of β-Gal in the brains of depressed mice was higher than that of normal mice. This phenomenon may be related to the persistent oxidative stress in the brains of depressed mice during the development of depression. This work reveals a positive correlation between depression and β-Gal activity in the brain, providing new ideas and targets for the diagnosis and treatment of depression.

Key Words: oxidative stress,depression,β-Galactosidase

Perturbation in mitochondrial quality control is associated with oxidative mitochondrial damage in patients with schizophrenia

Shuhui Li[a,1]（李书慧）, Xiaowen Hu[a,*], Chunling Wan[a,*]

[a] *Bio-X Institutes, School of Life Sciences and Biotechnology, Shanghai Jiao Tong University, Shanghai, 200030, China.*

**Correspondence email:lishuhui_0929@163.com;xiaowen@sjtu.edu.cn;clwan@sjtu.edu.cn.*

Abstract

Mitochondrial dysfunction has been suggested to play an important role in the pathology of schizophrenia (SZ). The mitochondrial quality control process, which can sense changes in cellular oxidative stress, is a key process for mitochondria to ensure the energy demand of cells. This study investigated the mitochondrial quality control in SZ patients with the aim to assess the mitochondrial dysfunction in multifaceted aspects including mitochondrial morphology, pathways involved and mitochondrial DNA maintenance. We found increased number but reduced size of mitochondria in SZ patients, suggesting a greater number of impaired mitochondria. Further, qPCR revealed higher expression levels in genes related to mitochondrial biogenesis, but lower levels in genes related to mitophagy, which were supportive to our findings on mitochondrial morphology. In contrast, the mtDNA copy number in SZ patients was not as comparably large as that in HC, and severe oxidative damage on mtDNA was found in SZ patients. These results suggest a dysregulation in the mitochondrial redox homeostasis in SZ, so our further investigations were focused on the antioxidant capacity, which revealed a decreased level of CoQ10 and reduced activity of SOD. To be noted, the SOD activity was positively correlated with the mtDNA copy number, suggesting the oxidative damage may account for the dysregulation of mitochondrial quality control. Finally, we explored the potential impact of mitochondrial dysfunction in terms of the energy metabolism and revealed a decreased *NDUFV1* gene expression level and increased lactate-to-pyruvate ratio in SZ patients. As a conclusion, our study suggests a perturbation in the quality control processes of mitochondria in SZ patients, which may be attributable to the mitochondrial oxidative damage and contribute to abnormalities in mitochondrial energy metabolism.

Curriculum vitae: Li Shuhui is a PhD candidate at the Bio-X Institutes of the School of Life Sciences and Biotechnology at Shanghai Jiao Tong University. Her research primarily focuses on the mechanisms of mitochondrial quality control, energy metabolism, and oxidative damage in schizophrenia. She has published two SCI papers as the first author.

Pyran compounds 7r reduces α-synuclein aggregation and protects neuronal activity in Caenorhabditis elegans by modulating the oxidative stress pathway and enhancing the activation of autophagy

Ruiting Han[1]（韩瑞婷）, Lu Luo[1], Na Feng[1,*]

School of Pharmacy and Food Engineering, Wuyi university, Jiangmen 529030, China

**Correspondence email: wyuchemfn@126.com*

Abstract

Abnormal accumulation of α-synuclein (α-syn) aggregates is a hallmark of various neurodegenerative disorders and dementias, especially Parkinson's disease (PD). Oxidative stress and autophagy deficits are intimately associated with α-syn aggregation and PD pathogenesis. Recent studies have demonstrated that pyran compounds possess free radical scavenging, antioxidant, and anti-inflammatory properties, along with beneficial effects in the context of neurodegenerative disorders. Consequently, the investigation of novel pyran compounds holds significant promise for the development of innovative therapeutic approaches for PD.

This study initially employed the ORAC assay to assess the antioxidant potential of pyran compounds in vitro, revealing that the pyran compound 7r exhibits robust antioxidant properties. Furthermore, in C. elegans models, 10 μM 7r was observed to markedly reduce levels of ROS and α-syn aggregation in the transgenic NL5901 strain, while also alleviating dopaminergic neuronal degeneration induced by 6-OHDA. These results suggest a neuroprotective effect of 7r, which is designated as NP7r. To elucidate the mechanisms underlying the protective effects of NP7r against PD, qPCR was conducted to assess genes associated with oxidative stress and autophagy. The results revealed that NP7r upregulated the mRNA levels of skn-1, gst-4, and gcs-1, as well as enhanced unc-51 and lgg-1 expression in NL5901 worms. Additionally, NP7r upregulated CCT family genes, with a more pronounced effect on cct-6, suggesting the activation of aggrephagy. Notably, the neuroprotective effects of NP7r were abolished upon RNAi targeting skn-1, unc-51, lgg-1 and cct-6, indicating that the capacity of NP7r to clear α-syn aggregation is dependent on these genes.

In summary, the pyran compound NP7r exhibits remarkable antioxidant and anti-PD activities. In the C. elegans PD model, this compound effectively reduces α-syn aggregation and elicits neuroprotective effects via the oxidative stress pathway and autophagy activation. This finding serves as a theoretical cornerstone for the development of novel anti-PD therapeutic agents.

Key Words: Parkinson's disease; pyran; oxidative stress; α-synuclein; autophagy

Restoring the redox and norepinephrine homoeostasis in mouse brains promotes an antidepressant response

Qi Ding[a]（丁琪）, Xin Wang,[a]* Ping Li,[a,c]* Bo Tang[a,b]*

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.*

[b] *Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.*

[c.] *College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic China*

**Correspondence email: lip@sdnu.edu.cn; xinwang@sdnu.edu.cn; tangb@sdnu.edu.cn*

Abstract

Effective diagnosis and treatments for major depressive disorder remains a major challenge, since diagnostic criteria overlap with other conditions and 50% of patients are resistant to conventional treatments. Emerging evidence has indicated oxidative stress and reduced norepinephrine as the key pathological features of depression. Herein, we constructed a smart organic small-molecule fluorescence based therapeutic system (Cou-NE-H_2O_2) for the diagnosis and treatment of depression targeted at restoring redox homeostasis and efficiently upregulating norepinephrine in the brain. Utilizing Cou-NE-H_2O_2, we could evaluate the depressive phenotype via fluorescence monitoring of the redox state in mouse brains. By reducing hydrogen peroxide and by continuously increasing norepinephrine, Cou-NE-H_2O_2 elicited synergistic antidepressant action. Furthermore, we identified that Cou-NE-H_2O_2 can promote the expression of genes such as Grin2a, Drd1, and Fxyd2 related to the cyclic adenosine monophosphate signaling pathway, upregulate glutathione and cysteine to alleviate oxidative stress and boost neuronal activity by enhancing the dopaminergic synapses, ultimately achieving an effective antidepressant response. Taken together, this work provides a new strategy for the evaluation of depression, appropriate treatments, and identifies the mechanisms underlying antioxidant and norepinephrine disorders in the brain as potential targets for the development of novel diagnostics and treatments for depression.

Sodium Danshensu Attenuates Blood-Brain Barrier Disruption and Hemorrhagic Transformation in Ischemic Stroke Rats with Acute Hyperglycemia: Involvement of ONOO--NLRP3 Inflammasome Pathway

Chen S[1]（陈霜）, Chen HS[1], Chen XM[1], Tsoi B[1], Shang A[1], Shen JG[1,2*]

[1]*School of Chinese Medicine, The University of Hong Kong*

[2]*The University of Hong Kong-Shenzhen Institute of Research and Innovation (HKU-SIRI), China*

**Correspondence email:u3007524@connect.hku.hk*

Abstract

Acute hyperglycemia occurs in 40% of ischemic stroke patients. Hyperglycemia is highly associated with increased brain damage, hemorrhage transformation (HT), mortality and poor functional recovery in ischemic stroke patients. Peroxynitrite plays an important role in the breakdown of blood–brain barrier (BBB) and the development of HT. We tested the hypothesis that Sodium Danshensu (SDSS), a representative active compound from a traditional Chinese Medicine (TCM) Danshen, could be used to protect the BBB, minimize HT, and improve neurological function by suppressing peroxynitrite-mediated Nod-like receptor protein 3 (NLRP3) activation. We used an experimental rat stroke model subjected to 90 min of middle cerebral artery occlusion plus 24 h of reperfusion with or without acute hyperglycemia. SDSS (20, 40, 60 mg/kg) was administrated via femoral vein at 2 h after MCAO cerebral ischemia.SDSS at high dosage significantly reduced the BBB damage, brain edema, and HT, enhanced neurological function, and reduced mortality rate in the ischemic stroke rats with hyperglycemia. SDSS reduced peroxynitrite and superoxide in vivo and in vitro. Furthermore, SDSS inhibited NLRP3 activity, reduced tight junction protein occludin nitration modification and preserved occludin and claudin-5 in the ischemic brains. Therefore, SDSS could attenuate hyperglycemia-mediated HT and improve the outcomes of ischemic stroke treatment possibly via inhibiting peroxynitrite-mediated tight junction degradation.

Superoxide anion-mediated mitochondrial dysfunction in the hippocampus of depressed mice revealed by fluorescent sensing and labeling strategies based on tandem activity

Xiwei Li[a]（李玺威）, Xin Wang,[a*] Ping Li,[a,c*] Bo Tanga,[b*]

[a] *College of Chemistry, Chemical Engineering and Materials Science, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Institutes of Biomedical Sciences, Shandong Normal University, Jinan 250014, P. R. China.* [b] *Laoshan Laboratory, 168 Wenhai Middle Rd, Aoshanwei Jimo, Qingdao 266237, Shandong.* [c.] *College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, People's Republic China*

**Correspondence email: xinwang@sdnu.edu.cn; lip@sdnu.edu.cn; tangb@sdnu.edu.cn*

Abstract

The molecular mechanisms underlying the origin of mitochondrial oxidative stress and subsequent excessive peripheral mitochondrial division in the hippocampus of depressed mice remain poorly defined. As the first reactive oxygen species produced in mitochondria, the concentration of superoxide anion ($O_2^{\bullet-}$) represents the level of oxidative stress directly, suggesting that $O_2^{\bullet-}$ may be involved in the excessive peripheral division of mitochondria in depression. Therefore, accurate in situ tracking of the level of $O_2^{\bullet-}$ in mitochondria is crucial and challenging to understand its role in mitochondrial peripheral fission. Here, we report a tandem active group- based sensing and labeling strategy fluorescent probe (**RB-FM**) for precisely tracking mitochondrial $O_2^{\bullet-}$ concentration. Probe **RB-FM** reacts with $O_2^{\bullet-}$ by forming a quinone methyl intermediate and covalently binds to the biological nucleophile in the near space and releases intense fluorescence. In situ imaging with the probe RB-FM revealed a significant increase in mitochondrial $O_2^{\bullet-}$ in the hippocampus of depressed mice. More importantly, we also observed elevated Ca^{2+} concentrations and decreased expression of enzymes involved in mitochondrial biogenesis in the hippocampus of depressed mice. Furthermore, the results of experiments showed that elevated neuronal Ca^{2+} resulted in a hyperoxia-dependent increase in mitochondrial peripheral fission and down-regulation of proteins involved in mitochondrial biogenesis.

Our work identifies a pathologic cascade in depression that begins with elevated calcium concentrations in hippocampal neurons, leading to upregulation of mitochondrial $O_2^{\bullet-}$ and oxidation of mitochondrial proteins, and ultimately to impaired mitochondrial function and reduced synaptic plasticity.

Synergistic effects of Tanshinone IIA sustained release nano particles on Parkinson's disease insults

Yuhao Kan[a,b#]（阚宇豪）, Zhirui Li[a#], Haoxiao Cheng[a], Yuming Zhao[a*]

[a] *Department of Pharmacology, School of Basic Medical Sciences, Capital Medical University, Beijing,100069, P.R. China*

[b] *Beijing Luhe Hospital affiliated to Capital Medical University, Capital Medical University, Beijing, 100069, P.R. China*

**Correspondence email: 2011228@ccmu.edu.cn；yumingzhao@ccmu.edu.cn*

Abstract

Tanshinone IIA (TIIA) exhibits promising neuroprotective effects for Parkinson's disease (PD). However, its clinical application is limited due to its short half-life and poor water solubility. This study aimed to develop an oral intestinal sustained-release formulation of TIIA using nanoparticles for effective drug delivery and enhanced druggability. The results demonstrated that TIIA-TPS-CSNPs had excellent water solubility and redispersibility. The release of TIIA was found to be more prominent in an alkaline environment, suggesting that it primarily occurred in the intestinal tract. Behavioral tests revealed that TIIA-TPS-CSNPs alleviated motor dysfunction in mice induced by MPTP. Nissl staining showed improvements in cell swelling, pyknosis, and cell death following treatment with TIIA-TPS-CSNPs. Moreover, TIIA-TPS-CSNPs significantly enhanced the fluorescence intensity of tyrosine hydroxylase (TH) and increased the number of TH-positive cells. Biochemical analysis indicated that TIIA-TPS-CSNPs significantly increased superoxide dismutase2 (SOD2) activity and GSH content. Western blot analysis revealed that TIIA-TPS-CSNPs inhibited oxidative stress by regulating the Nrf2 pathway and the AKT/FOXO1/SOD2 pathway. In conclusion, our nano drug delivery system improved drug bioavailability and enhanced druggability. Furthermore, TIIA-TPS-CSNPs exhibited a significant protective effect against nerve damage by inhibiting oxidative stress, thereby displaying a synergistic effect.

TFR Enhances α-Synuclein-mediated Ferroptosis in the Hippocampus of Parkinson's Disease Dementia

Lijun Zhao[1]（赵丽君）, Mengzhu Li[2], Qizhang Wang[1*], Meiling Zhu[*2]

1. Shenzhen Hospital of Integrated Traditional Chinese and Western Medicine, Shenzhen, 518104

2. The fourth Clinical Medical College of Guangzhou University of Chinese Medicine, Shenzhen, 518033

**Correspondence email: meilingzhu2020@126.com；qizhangwang@126.com*

Abstract

Parkinson's Disease Dementia (PDD) is a cognitive disorder that occurs in patients with Parkinson's disease (PD). The characteristic hallmark of PDD is the abnormal accumulation of α-synuclein (α-syn) in the hippocampus neurons. Recent research indicates that α-synuclein plays a role in initiating ferroptosis and is significantly associated with the progression and onset of Parkinson's Disease Dementia (PDD). As a critical protein in iron metabolism, the transferrin receptor (TFR) regulates iron accumulation, which allows it to modify ferroptosis. Nonetheless, the link between TFR and the unusual buildup of α-syn remains unexplored. This study confirmed that α-syn could induce ferroptosis in the HT22 cell model and A53T animal. The effect of TFR on ferroptosis due to abnormal aggregation of α-syn was further studied by over-expressing or knocking down TFR. Research findings indicate that the high expression of TFR can promote aberrant α-syn aggregation, exacerbating α-syn-mediated ferroptosis. Our research can yield novel concepts for the early diagnosis and treatment of PDD. Discovering and focusing therapies on new targets for PDD is also essential.

Key Words: Parkinson's Disease Dementia; Parkinson's Disease; TFR; α-synuclein; Ferroptosis

The beneficial effect of Angong Niuhuang Pill (AGNHP) on ischemic stroke via the regulation of gut microbiota

Shang Ao[1]（商奥）, Shen Jiangang[1*]

1 School of Chinese Medicine, State Key Laboratory of Pharmaceutical Biotechnology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, 999077;

**Correspondence email: shenjg@hku.hk*

Abstract

Stroke is a medical emergency that seriously endangers human health with high mortality and disability rate. Clinically, gastrointestinal dysfunction has been observed in a high proportion of stroke patients, suggesting that gut microbiota may be a target for stroke prophylaxis and treatment. Angong Niuhuang Pill (AGNHP) is a well-known traditional Chinese medicine formula, believed to be effective in treating stroke, and its heavy metal components realgar and cinnabar were found to be essential and mainly distributed in the intestine.

In this study, we investigated the protective effects of AGNHP on stroke and gut microenvironment through the brain-gut axis. The results showed that AGNHP treatment significantly reduced infarct size and improved neurocognitive function. Also, AGNHP protected the morphological structure and integrity of intestine, including restoring the expression of intestinal tight junction proteins occludin and claudin-5, as well as reducing D-lactate, lipopolysaccharide and diamine oxidase in systemic circulation. Further, we found that AGNHP effectively improved the oxidative stress of intestine, like reducing the expression of 3-nitrotyrosine, and down-regulated pro-inflammatory factors interleukin (IL)-6, IL-1β, and TNF-α, etc. Moreover, 16S rRNA analysis showed that AGNHP treatment had a positive regulatory effect on intestinal bacterial composition after stroke, such as increase the proportion of probiotic *Lactobacillus* and decrease pathogenic *Escherichia*.

Therefore, our study verified the therapeutic effect of AGNHP on stroke from the perspective of regulating gut microbiota, and provided a theoretical basis for its further clinical application.

Key Words: ischemic stroke, Angong Niuhuang Pill, gut microbiota, oxidative stress, inflammation

The Deubiquitination of Erg1 by USP7 Regulates Nrf2 Redox Balance and Mitigates Fluoride-Induced Neurotoxicity

Wenjin Qiu（仇文进） ,Liangzhao Chu

The Affiliated Hospital of Guizhou Medical University

Department of Neurosurgery, The Affiliated Hospital of Guizhou Medical University,

Guiyang City, Guizhou Province, CHINA

**Correspondence email: wenjinqiu@gmc.edu.cn*

Abstract

Background: Excessive long-term fluoride intake causes multi-organ damage, including neurotoxicity, primarily through oxidative stress. Nuclear factor erythroid 2-related factor 2 (Nrf2) is crucial in the antioxidant response, while USP7 (ubiquitin-specific protease 7) regulates target protein stability through deubiquitination, linked to neurodegenerative diseases. This study explores USP7's role in Erg1 deubiquitination and its effect on Nrf2 redox balance and fluoride-induced neurotoxicity.

Methods: In vitro and in vivo models were used. Single-cell sequencing analyzed transcriptomic changes in the prefrontal cortex post-fluoride intoxication. USP7's role in Erg1 stability was assessed through overexpression and knockdown experiments. The impact of the USP7-Erg1 axis on Nrf2 signaling and downstream antioxidant genes was measured via Western blot, qPCR, and immunofluorescence. An Erg1 overexpression transgenic mouse model exposed to fluoride was used to evaluate neuroprotection by examining neuronal function and morphology.

Results: Fluoride intoxication significantly decreased Erg1 transcription and protein levels, with Erg1 undergoing ubiquitin-proteasome degradation. USP7 stabilized Erg1 via deubiquitination. Transcriptomic analysis showed significant changes in Nrf2-mediated oxidative stress pathways post-fluoride exposure. Erg1 overexpression activated Nrf2 expression, enhancing antioxidant gene expression and reducing ROS levels. In the mouse model, Erg1 overexpression alleviated neurotoxicity, promoted Nrf2 pathway activation, and improved oxidative stress.

Conclusion: This study identifies USP7 as a key regulator of the Nrf2 signaling pathway through Erg1 deubiquitination, highlighting its protective role in fluoride-induced neurotoxicity. The USP7-Erg1-Nrf2 axis presents a promising therapeutic target for preventing and treating fluoride-induced neurotoxicity.

Key Word：USP7； Erg1； Nfr2；redox balance；fluorosis； neurotoxicity

The effect and mechanism of knockdown Ferroportin1 in microglia on cerebral ischemia-reperfusion injury

QiaoYa Zhao（赵悄雅）, YanZhong Chang

The Laboratory of Iron Metabolism, College of Life Science, Hebei Normal University, Shijiazhuang 050024, China

**Correspondence email: Zhao77u@outlook.com*

Abstract

The mechanisms of ischemia/reperfusion (I/R) injury are complex, with the inflammatory response being an important part of the cascade of responses that contribute to cerebral ischemic injury. Microglia are resident immune cells in the central nervous system (CNS) of the brain, participate in the innate and acquired immune response of the brain, and play a key role in the inflammatory response following the response to I/R injury. Brain iron homeostasis is essential for the development of the central system and the maintenance of normal physiological functions. Brain iron imbalance has been observed to occur in a variety of neurological disorders. Ferroportin1 (FPN1), the only known iron export protein, is highly expressed in a variety of neuronal cells, including microglia, and is critical for iron metabolic homeostasis in the brain. The absence of FPN1 in microglia causes iron to be deposited in microglia where it cannot be excreted, and intracellular iron levels are altered. Although a variety of mechanisms by which microglia regulate I/R injury have been identified, the role of changes in iron levels in microglia on microglia polarization, and in I/R injury, has not been reported in detail. This article discusses the effects of altered iron metabolism in microglia on ischemic stroke and its mechanisms, with the aim of providing new targets for intervention in the treatment of secondary brain injury after ischemic stroke.

Synthesis and characterization of Tanshinone IIA nanoparticles for the treatment of cerebral stroke

Sihan Wang[a]（王思涵）, *Qiming Gao*[a], *Libo Du*[b], *Yang Liu*[b], *Yuming Zhao*[a*]

[a] *Department of Pharmacology, School of Basic Medical Sciences, Capital Medical University, Beijing, 100069, P.R. China.*
[b] *State Key Laboratory for Structural Chemistry of Unstable Species, Center for Molecular Science, Institute of Chemistry, Chinese Academy of Science, Beijing, 100190, P.R. China*

**Correspondence email: yumingzhao@ccmu.edu.cn*

Abstract

Purpose Tanshinone II A (TIIA) is a multiple functional neuroprotectant which has promising antioxidant effects for ischemic stroke intervention. TIIA attenuates oxidative stress by enhancing activities of superoxide dismutase and decreasing levels of malonaldehyde, nitrogen monoxide and inducible nitric oxide synthase expression. However, its poor water solubility and short half-life limits its clinical application. Nano-drug delivery systems can improve the absorption of poorly soluble oral drugs and increase the rate of drug passage through the blood-brain barrier. Chitosan (CS) is a kind of natural polymer composed of glucose monomer as a structural unit. It is prepared by chitin deacetylation in nature. In this study, low molecular chitosan was linked to α-tocopheryl succinate (TPS) to synthesize the nano-carrier of chitosan-α-tocopheryl succinate (CS-TPS). **Methods** TIIA was encapsulated by the CS-TPS nanocarrier. The Chemical structure of TIIA nano preparation was observed by infrared spectra and ^{1}-H nuclear magnetic resonance. The particle size and zeta potential of CBSA-PEG-TIIA-NPs were measured by laser dynamic light scattering. The morphology of CBSA-PEG-TIIA-NPs was observed by transmission scanning electron microscope. And the entrapment efficiency and drug loading of CS-TPS-TIIA was assayed by ultraviolet spectrum. **Results** The infrared spectra showed that the absorption peak intensity of CS-TPS at C-H and C=O increased, indicating the successful combination of TPS and CS to form polymer. The proton magnetic resonance analysis showed that the chemical shift strength of CH_2 in CS-TPS was significantly stronger than that of CS, which also indicated that TPS and CS were successfully combined. Scanning electron microscope showed that CS and CS-TPS-TIIA were suborbicular and monodisperse particles. The results of laser dynamic light scattering show that the diameters of CS-TPS and CS-TPS TIIA were 72.9 nm and 112.1 nm, which indicated that TIIA was successfully encapsulated. In addition, it can be observed that both CS-TPS and CS-TPS-TIIA have stably and well dispersed in water. The concentration of TIIA in the CS-TPS-TIIA was 5 mg/ml by ultraviolet spectrum. In addition, calculated by ultraviolet spectrum, the entrapment efficiency and drug loading of TIIA were 98.2±1.5% and 15.2±1.6%. Furthermore, the nanoparticles were positively charged which facilitated TIIA to penetrate across the negatively charged blood brain barrier (BBB). **Conclusions** TIIA was successfully encapsulated by the nanocarrier of CS-TPS, which might enhance the transport of TIIA across BBB with high biological safety. CS-TPS nanocarrier system might have great advantages to enhance the bioavailability by enhancing the solubility and the ability to across the BBB of the candidate neuroprotectants in stroke intervention.

Fluorescence-enhanced detection of hypochlorite based on in situ synthesis of functionalization-free carbon spheres

Tianhong Liu[a]（刘天鸿）, Qiang Zhang[a,b] , Mingtai Sun[a], Xiangyang Hao[b], Suhua Wang[a]

a. School of Environmental Science and Engineering, Guangdong University of Petrochemical Technology, Maoming 525000, China

b. Engineering Research Center of Ministry of Education for Geological Carbon Storage and Low Carbon Utilization of Resources, Beijing Key Laboratory of Materials Utilization of Nonmetallic Minerals and Solid Wastes, National Laboratory of Mineral Materials, School of Material Sciences and Technology, China University of Geosciences, Beijing 100083, China

**Correspondence email: 15666873790@163.com*

Abstract

A considerable number of diseases have been linked to the presence of Hypochlorite (ClO^-) in the environment. Although abundant organic molecule-based probes have demonstrated high sensitivity and selectivity for ClOresponse, they often suffer from limitations including tedious preparation steps, poor water solubility, and the use of toxic solvent. In this work, we designed a hydrothermal reaction based method for novel carbon spheres （ CS ） synthesis, which demonstrated selective fluorescence response to ClO^- without further functionalization. In the presence of ClO^- , the obtained micro-size CS that initially displayed very weak fluorescence experienced a significant fluorescence enhancement in the blue channel, and a linear response range of 2-110 μM with detection limit of 10.7 nM could be achieved. In addition, Hoffmann degradation-involved reaction was hypothesized to be the mechanism behind this fluorescence response in the system, which was partially confirmed by various experiments including XPS, UV–vis and FTIR. Based on the mechanism verification, a portable sensing platform for the on-site detection of ClO^- was designed using CS for the rapid and selective fluorescence response. Moreover, the visual quantitative fluorescence sensor platform has been successfully employed in the detection of ClOin environmental water samples, thereby demonstrating its potential for use in portable detection.

Liver injury induced by subchronic respiratory exposure to lithium nickel cobalt manganese oxide in mice

Yongqin Xia（夏永钦） Ruirui Wu Jinghui Qu Xiangbo Xu Junyi Wang Yuxin Hu Jingbo Pi Yuanyuan Xu

China Medical University

**Correspondence email: xia2000_qin@163.com*

Abstract

Objective: Lithium Nickel Cobalt Manganese Oxide ($LiNi_xCo_yMn_{1-x-y}O_2$，NMC) is a new type of cathode material for lithium-ion batteries. The aim of this study was to investigate the characteristics of liver injury by respiratory NMC exposure in mice and the role of NRF2, a master regulator in antioxidative defense in it. Methods: A 90-day model of subchronic exposure to NMC was established in 8-week-old wild-type C57BL/6J male mice. After exposure, tissues were weighed and serum ALT and AST levels were measured. The liver morphology was observed by H&E staining. The co-regulatory pathways of Co, Li, Mn and Ni were analyzed using CTD. The expression level of Nrf2 and its antioxidant downstream gene and the level of MDA in liver tissue were detected. Results: NMC exposure resulted in a significant increase in liver coefficients ($P < 0.05$), hepatocyte swelling, granuloid degeneration, and increased inflammatory cell infiltration. ALT and AST levels were not significantly changed. CTD analysis found that the four metal elements jointly regulated the oxidative stress-related pathway enrichment genes, including the classic antioxidant gene Nrf2 and its downstream genes. The functional enrichment analysis showed that the interaction genes of the four metal elements were strongly enriched in oxidative stress-related pathways. The mRNA expression levels of *Nrf2* and its downstream gene *Nqo1* and *Gclc* were significantly increased in liver ($P < 0.05$), while the expression levels of *Hmox1* and Gclm showed an increasing trend but no statistical difference. The expression of NRF2 protein was also significantly increased. There was no statistical difference in the increase of MDA level in liver. Conclusion: Respiratory NMC exposure causes damage and disrupts redox homeostasis in the liver.

Acknowledgement: NSFC82241090

Key Words: Lithium Nickel Cobalt Manganese Oxide, liver injury, NRF2

Preparation of baicalin self-microemulsified preparation and study on its radiation protection effect

Liu Xinran（刘欣然）, Gao Zhonghong, Li Hailing

Huazhong University of Science and Technology.430074

**Correspondence email: lele15506526107@163.com*

Abstract

In recent years, with the development of nuclear technology, the risk of radiation damage is increasing. Traditional Chinese medicine can prevent radiation damage by reducing DNA damage and oxidative stress. Many traditional Chinese medicine prescriptions have been used to reduce radiation-induced damage in clinical application. Baicalin (BA) is a flavonoid extracted from the root of scutellaria baicalensis, which has anti-inflammatory and antioxidant effects. However, due to its molecular structure, the solubility and bioavailability of BA is low. Therefore, some preparations are needed to promote the absorption of BA. In our study, the formula was screened by solubility investigation and pseudo-ternary phase diagram, optimized by star design and effect surface method, and innovatively added ginsenoside (GS), a natural surfactant, to reduce surface tension and promote baicalin absorption, and at the same time play an anti-inflammatory and immune role. Based on this, self-microemulsion drug delivery system of baicalin (BA-GS-SMEDDS) was constructed. The properties of BA-GS-SMEDDS were studied in vitro and in vivo through particle size distribution, encapsulation rate, pharmacokinetics and other indicators, and a radiation model was constructed to explore the radiation protection effect of BA-GS-SMEDDS. The BA-GS-SMEDDS spontaneously formed O/W type microemulsion with a particle size of 21.03 nm by absorbing water in the gastrointestinal tract after oral administration. The average encapsulation rate of BA-GS-SMEDDS was 95.47%, and the stability was good. Compared with free drugs, the bioavailability of BA was increased by 4.38 times, which promoted the absorption of BA and prolonged the action time of BA. At present, the prepared BA-GS-SMEDDS have been preliminarily shown to have certain antioxidant effects on the constructed radiation model. The BA-GS-SMEDDS prepared in our study improved the bioavailability of the main drug BA and promoted its absorption in the body, and it also showed antioxidant effect in the damage caused by radiation.

Biyuantong decoction reduces postoperative recurrence of chronic rhinosinusitis by inhibiting ferroptosis

Yinyin Yao[1,2]（姚茵茵）, Zhouzhou Ye[2], Judan Xu[2], Shanshan He[1,2], Luo Lin[2], Guoqing Wu[3], Chunlian Zhong[2], Yusheng Lu[2*], Mingqing Huang[1*], Yuying Ye[3*]

[1] *College of Pharmacy, Fujian Key laboratory of Chinese Materia Medica, Fujian University of Traditional Chinese Medicine, Fuzhou 350122, China*

[2] *Fujian-Taiwan-Hongkong-Macao Science and Technology Cooperation Base of Intelligent Pharmaceutics, College of Material and Chemical Engineering, Minjiang University, Fuzhou, Fujian 350108, China*

[3] *Department of Otorhinolaryngology, Affiliated People's Hospital (Fujian Provincial People's Hospital), Fujian University of Traditional Chinese Medicine, Fuzhou, 350004, China*

**Correspondence email: lu_yu_sheng@126.com ; hmq1115@126.com；334515834@qq.com*

Abstract

Background: Ferroptosis is a form of regulated cell death that depends on iron accumulation and is driven by lipid peroxidation, but its regulatory mechanisms in chronic rhinosinusitis (CRS) are not well understood.

Methods: Biyuantong decoction(BYT) was used to treat HNEPC cells, followed by RNA sequencing to screen for genes significantly associated with ferroptosis. Cells were treated with ferroptosis inducers, and the mRNA expression of the selected genes was detected using qRT-PCR. Then, we studied the changes in total reactive oxygen species (ROS) and lipid peroxidation levels in HNEPC cells under the action of ferroptosis inducers and BYT. Finally, Western blotting was used to detect the expression of ferroptosis-related proteins to verify the effect of BYT in inhibiting ferroptosis.

Results: RNA sequencing identified significantly differentially expressed genes in BYT treatment before and after, including HO-1, FTH1, and SLC7A11, which are closely related to ferroptosis. qRT-PCR confirmed that the mRNA levels of related genes increased after BYT treatment, which was consistent with the results of RNA sequencing. Furthermore, we found that BYT significantly suppressed the levels of total ROS and lipid peroxidation induced by ferroptosis. Mechanistically, BYT effectively counteracted the downregulation of protein levels of FTH1, SLC7A11, and GPX4 induced by ferroptosis.

Conclusion: BYT exhibits potential in reducing postoperative recurrence of CRS by inhibiting ferroptosis through upregulation of anti-ferroptosis factors such as GPX4.

Key Words: Chronic rhinosinusitis，Biyuantong decoction，Ferroptosis

Coptisine Reduces Transformation Process From Chronic Atrophic Gastritis to Gastric Cancer via Inhibiting Hepcidin Expression

Yashuo Zhao[1,2,3†]（赵亚硕）, Hongyu Ma[1,2†], Bo-liang Li[1,2,3†], Yu-hui Gao[1,2,3], Yujing Gou[1,2,3†], Jie Wang[1,2], Yanru Cai[1,2], Yan Han[1,2], Zheng Zhi[1,2*], and Qian Yang[1,2*]

[1] *Hebei Key Laboratory of Turbidity Toxin Syndrome, Hebei University of Chinese Medicine, Shijiazhuang, 050013, China*

[2] *Key Laboratory of Integrated Chinese and Western Medicine for Gastroenterology Research, Hebei University of Chinese Medicine, Shijiazhuang, 050013, China*

[3] *Hebei Technology Innovation Center of TCM Combined Hydrogen Medicine, Hebei University of Chinese Medicine, Shijiazhuang 050200, China*

**Correspondence email: zys870207@126.com, yang0311qian@126.com.*

Abstract

Background: Chronic atrophic gastritis (CAG) is often associated with inflammation and is also considered a high-risk factor for gastric cancer (GC), but the detailed pathogenesis is still unclear. **Objectives:** The aim of this study was to clarify whether hepcidin is involved in the process of "inflammation-cancer" transformation and the protective effect of the Chinese herb of Coptisine. **Methods:** Non-atrophic gastritis (NAG) and chronic atrophic gastritis (CAG) patients' serum and gastric mucosal tissue sections were collected for proteomics analysis and immunofluorescence. The CAG rat was established using MNNG combined with an irregular diet. GES-1 cells were also used to study CAG *in vitro*. **Results:** Proteomics analysis showed that CAG patients were accompanied by abnormal iron metabolism, ferroptosis, inflammation and gastrointestinal tumourigenesis *et al*. Immunofluorescence results indicated that hepcidin is highly expressed in gastric tissues of CAG and GC patients. Coptisine inhibited ferroptosis in gastric tissue of CAG rats by improving mitochondrial structure, upregulating glutathione peroxidase-4 (GPX-4) and downregulating 4-hydroxynonenal (4-HNE). Coptisine reduced CAG-induced iron deposition by inhibiting hepcidin and ferritin light chain (FTL) and increasing ferroportin 1 (FPN1) levels. Furthermore, gastric tissue from CAG patients showed M1-type macrophage activation, and Coptisine treatment inhibited the release of pro-inflammatory factors and markers of pre-cancerous tumours. In addition, the cell experiments further confirmed that hepcidin was able to exacerbate MNNG-induced damage, ferroptosis, and elevated labile iron pools (LIPs) in GES-1 cells, and that Coptisine could specifically bind hepcidin to exert a protective effect. **Conclusion:** Our results showed that Coptisine could inhibit the process of "inflammation-cancer" transformation by attenuating hepcidin-induced ferroptosis in CAG.

Key Words: Chronic atrophic gastritis， Hepcidin， Ferroptosis， Transformation of "inflammation-cancer"

Dihydroisotanshinone I functions as an agonist of TRPV1 to alleviate lipopolysaccharide-induced neuroinflammation in vitro and in vivo

Nan Xu [1]（徐楠）, Shuli Li [1], Hiotong Kam [1], Yulin He [1,2], Pengu Lao [1], Xin Nie [1], Simon Ming-yuen Lee [1,2,3]

[1] *State Key Laboratory of Quality Research in Chinese Medicine and Institute of Chinese Medical Sciences, University of Macau, Macao, China*

[2] *Department of Food Science and Nutrient, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China*

[3] *Research Centre for Chinese Medicine Innovation, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, China*

**Correspondence email: yc17526@um.edu.mo*

Abstract

Neuroinflammation and oxidative stress mediated by microglia are inevitable and important pathological processes in several types of disorder of the central nervous system (CNS). Transient receptor potential vanilloid type 1 (TRPV1), a nonselective cationic channel with high permeability to Ca^{2+}, has recently been demonstrated to have functionally expressed in glial cells and might exert a positive action over neuroinflammatory processes. However, there are no approved drugs specifically targeting TRPV1 for CNS diseases. Dihydrotanshinone I (DHT) is a representative component separated from Salvia miltiorrhiza Bunge (Danshen) with multiple activities, whereas its effect and underlying mechanism against neuroinflammation remain unclear. Here, we aim to elucidate the potential protective effects of DHT as a TRPV1 activator on lipopolysaccharide (LPS)-induced neuroinflammation in BV-2 microglial cells and zebrafish. First, our results performed that DHT had a strong and stable binding with TRPV1 and obviously induced the calcium influx in HEK293-hTRPV1 cell, which indicated that DHT was able to be a promising TRPV1 agonist. Then, DHT significantly decreased the NO production, as well as the mRNA expression of iNOS, TNF-α, IL-1β and IL-6 in LPS-stimulated BV-2 microglial cells. And the inhibitory effect of DHT on NO production was superior to that of the well-known TRPV1 agonist, capsaicin. Furthermore, DHT provided protective actions against LPS-induced elevated mRNA expression of TNF-α, IL-1β and IL-6 in the head of zebrafish larvae and recruitment of neutrophils in the zebrafish brain. Moreover, DHT conferred indirect anti-oxidative effects via quenching ROS. Nevertheless, SB-366791, the antagonist of TRPV1, abrogated the benefits derived from DHT. Taken together, the results suggest that DHT exerts anti-neuroinflammatory and antioxidant effects by activating TRPV1, providing important evidence for its potential as a therapeutic agent for neuroinflammation-associated CNS disorders.

Key Words:

Dihydrotanshinone I; TRPV1; Microglia; Anti-neuroinflammation; Anti-oxidation

RSM for Revealing Traditional Chinese Medicine's Yun Qi Wisdom Based on the Theory of Superstrings

Chen Jiulong（陈久龙）

Dahua Group Co., Ltd. 116032

**Correspondence email: 3770216547@qq.com*

Abstract

The "Yuan of superstring " in the superstring theory, which is at the forefront of modern science, the "Yuan of life" in the redox balance theory, which is at the forefront of modern life science, and the "Yuan of Shen Qi" in the traditional Chinese medicine “Yun Qi” wisdom with a history of more than 5000 years, “Yi Ming Tong Shi”,“QI Zhi Yi Ye”, All are “Zhi Yi”, All are “Zhi Mei”. The three are combined into one, it can “Kai Xian” extraordinary prospects for the way of thinking about life and health for humanity today.

Key Words: Yuan. The Yuan of superstring. The Yuan of life. The Yuan of Shen Qi. Kai Xian. Zhi Yi. Zhi Mei.

A phosphatase-like nanomaterial promotes autophagy and reprograms macrophages for cancer immunotherapy

Su Li[1,2,*]（李苏）, Guofang Zhang[1], Yang Li[1,*]

1 Laboratory of Immunology and Nanomedicine, Laboratory of Inflammation and Vaccines, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, P.R. China

2 College of Natural and Life Sciences, Paris Lodron University of Salzburg, Salzburg 34 5020, Austria

**Correspondence email: s.li@siat.ac.cn; yang.li@siat.ac.cn*

Abstract

The imbalanced redox microenvironment is not only a crucial factor for tumor growth and progression, but also one of the primary causes of tumor-induced immunosuppression. Therefore, maintaining the redox balance in tumors to reduce immunosuppression has become an important strategy for cancer treatment. Considering the complexity of the redox microenvironment, multiple signaling pathways and regulatory mechanisms are usually involved. Therefore, we need to develop effective drugs that can act on multiple targets simultaneously to achieve a more comprehensive regulation of the redox balance, achieving alleviated immunosuppression for effective tumor inhibition.

$LaNiO_3$ (LNO), as a perovskite nanozyme, has peroxidase activity. Although it has been reported that Lanthanide-doped nanoparticles can reduce intracellular ATP levels, the underlying mechanism remains unclear. We discovered that $LaNiO_3$ possessed the ability to bind with ATP for phosphate hydrolyzation, thus working as an alkaline phosphatase and leading to cellular autophagy. In this direction, we have studied its role in modulating tumor-associated macrophages (TAMs), which usually exhibit M2-like polarization and are metabolized by oxidative phosphorylation. We found that $LaNiO_3$ can activate AMPK-mTOR signaling pathway through hydrolysis of ATP and protein dephosphorylation, promoting macrophage autophagy and reprogramming for effective cancer immunotherapy.

In summary, LNO holds a dual-catalytic activity. LNO directly engages in redox reactions, thereby directly alleviating oxidative stress and immunosuppression. It also regulates the intracellular AMPK-mTOR signaling pathway via ATP hydrolysis, further decreasing ROS levels and indirectly mitigating oxidative stress and immunosuppression. The dual-catalytic activity of LNO enables a synergistic and multi-targeting approach for cancer treatment with contribution of the maintenance of the redox balance in tumor microenvironment.

In situ nitric oxide production for selective S-nitrosation as a promising synergistic cancer treatment strategy

Chen Zhang（张宸）, Hui Ye, Duorui Ji, Cunrui Li, Hongyu Li,Jianbing WU,* Zhangjian Huang*

State Key Laboratory of Natural Medicines, China Pharmaceutical University.

**Correspondence email: chenzhang98@stu.cpu.edu.cn*

Abstract

Protein S-nitrosation (SNO) is a crucial post-translational modification. However, how to use medicinal chemistry methods to achieve selective S-nitrosation modulation in disease treatment remains largely unexplored.[1] Herein, we developed a warhead-based selective kinase nitrosation strategy by designing and synthesizing in situ NO-releasing warheads. Specifically, Compound **SSNO1** effectively bound to the kinase, and released NO in situ. This process achieved selective nitrosation of BTK at Cys527.

This selective S-nitrosation paradigm represents an example of the regulation of the post-translational modification crosstalk between nitrosation and phosphorylation. **SSNO1** exhibited an acceptable PK profile ($T_{1/2}$=2.53 h) and superior in vivo antitumor activity compared to **Ibrutinib**, with potential for further development as a clinical drug. These results suggested that this strategy not only introduces a novel concept in the selective regulation of protein nitrosation but also offered a new perspective for disease intervention and rational drug design.

Key Words: Protein S-nitrosation, Small-molecule inhibitor, Selectivity, Nitric oxide, Crosstalk, Anti-lymphoma

liver-targeted plasmid lipid nanomedicine treats liver fibrosis by ROS elimination

Zhengxun Liu（刘正汛）, Yan-Zhong Chang

Hebei normal university, 050024, 20 South Second Ring Road East, Shijiazhuang province, China;

**Correspondence email: liuzx1332@foxmail.com*

Abstract

Liver fibrosis is considered to be a reversible case physiological process during the progression of chronic diseases, and ROS-mediated mitochondrial autophagy and inflammation are important causes of liver fibrosis; elimination of excessive ROS and enhancement of antioxidant capacity are the keys to treating liver fibrosis. In this experiment, a liver-targeted plasmid lipid nanomedicine was developed for liver fibrosis treatment. Using ionizable cationic phospholipids with high safety, combining them with positively charged phospholipids and helper phospholipids as the core of polymerized nucleic acids, and traditional three-component phospholipids as the shell, liposome-targeted drugs capable of stable loading of plasmid DNA were obtained by wrapping through extrusion homogenization, and were successfully targeted to the liver to express the relevant proteins that inhibit oxidative stress and effectively reduce intrahepatic ROS. This experiment demonstrated that plasmid lipid nanomedicine is a potential new approach for the treatment of liver fibrosis by scavenging ROS and inhibiting inflammation and thus is preventing the progression of liver fibrosis.

Key Words: ROS, liver fibrosis, hepatocyte targeting, LNP

NOS-like activity of CeO_2 nanozymes contributes to diminishing the vascular plaques

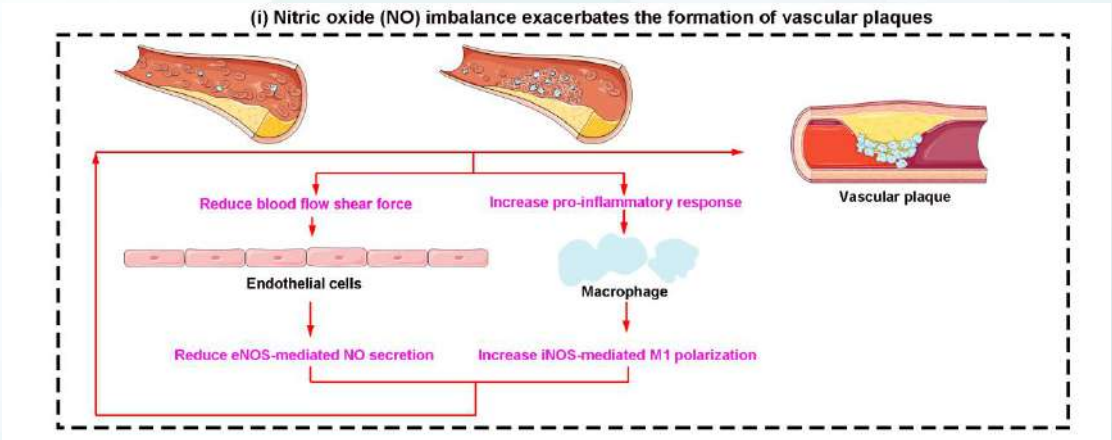
Yuxiang Sun [a] （孙玉祥）,Li Xu *,[a]

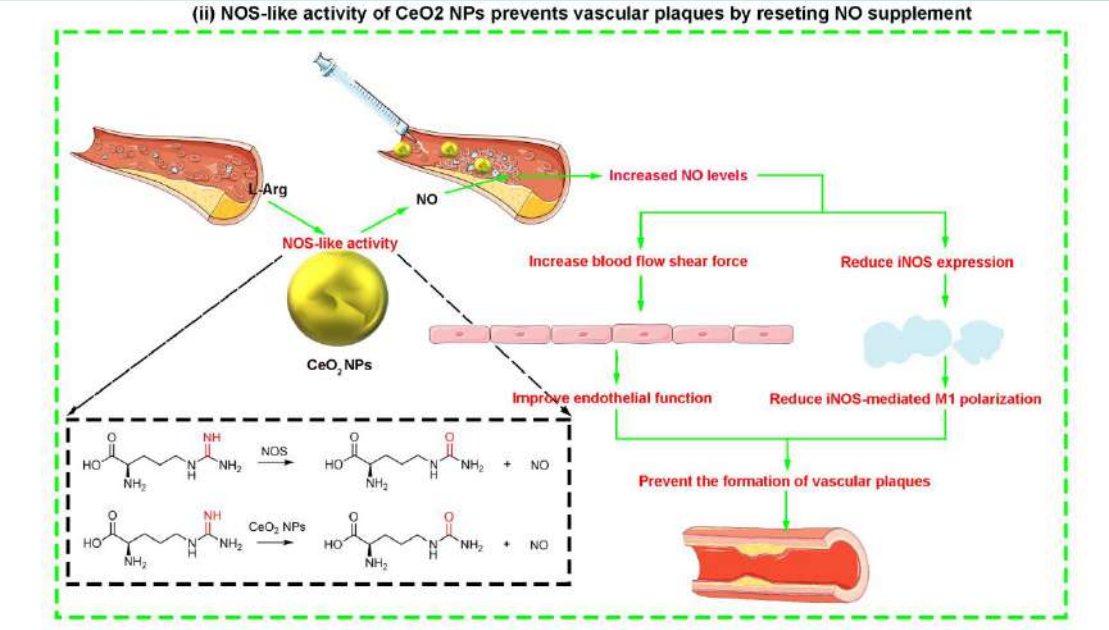
Yangzhou University

**Correspondence email: bsunyuxiang@126.com*

Abstract

Ceria nanoparticles (CeO_2NPs) exhibit great potential in cardiovascular disease and nonalcoholic fatty liver disease due to its excellent antioxidant capacity. However, the profitable effect of CeO_2NPs on many diseases is almost all attributed to the regulation of ROS. Apart from the general antioxidant function, there seems to be no more distinct mechanism to reflect its unique multi-disease improvement effect. Here, we for the first time reveal a new discovery of CeO_2NPs in mimicking nitric oxide synthase (NOS) by catalyzing L-arginine (L-Arg) to produce nitric oxide (NO) or the derivatives. NOS-like activity of CeO_2NPs is original and associated with multiple factors like substrate concentration, pH, temperature and time, etc. where oxygen vacancy ratio plays a more critical role. Meanwhile, NOS-like activity of CeO_2NPs successfully elevates NO secretion in endothelial cells and macrophages without expanding eNOS/iNOS expression. Importantly, NOS-like activity of CeO_2NPs and the responsive endogenous NO promote the re-distribution of blood lipids and stabilize eNOS expression but suppress iNOS, thus collectively alleviate the accumulation of vascular plaque. Altogether, we provide a new angle of view to survey the outstanding potential of CeO_2NPs, apart from the inevitable antioxidant capacity, the covert but possible and more critical NOS-like enzymatic activity is more noteworthy.





Scheme. (i) illustrates that the deposition of lipids and macrophages on the vascular wall can lead to abnormal NO secretion mediated by eNOS in endothelial cells and exacerbate iNOS-mediated pro-inflammatory responses in macrophages, which in turn feedback promotes the formation of vascular plaques. (ii) illustrates that CeO2NPs derived NO by the NOS-like activity can prevent vascular plaque formation via improving endothelial cell function and macrophage function. CeO2NPs simulates the activity of NOS to elevate NO level in serum. This exogenous way to supplement endogenous NO levels continuously can change the re-distribution of blood lipids as well as cell function by altering blood flow status including blood flow shear force

Key Words: Nitric oxide synthase, Ceria nanoparticles, Nitric oxide, Vascular plaques

Therapeutic effect of PN-CeO_2 on atopic dermatitis by regulating oxidative stress in keratinocytes and macrophages

Ruimin Bai[1]（白瑞敏）, Jiankang Liu[1,2,3], Yan Zheng[1*],

[1] *Department of Dermatology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China;*
[2] *Center for Mitochondrial Biology and Medicine, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an 710061, China;*
[3] *School of Health and Life Sciences, University of Health and Rehabilitation Sciences, Qingdao 266071, China*

**Correspondence email: zenyan66@126.com*

Abstract

Atopic Dermatitis (AD) is a prevalent inflammatory skin condition. Oxidative stress plays a significant role in AD, and nanoceria possesses redox regulation capabilities. Thus, we explored its potential use in AD treatment. We created a porous ceria nanorod (PN-CeO_2) with the ability to scavenge reactive oxygen species (ROS). In vitro experiments demonstrated that PN-CeO_2 could decrease ROS and influence cytokine expression in TNFα-stimulated keratinocytes, LPS-stimulated M1 macrophages, and IL4-stimulated M2 macrophages. The cytokine expression of HaCaT cells was also affected by the conditioned medium of M1 type macrophages incubated with PN-CeO_2. PN-CeO_2 exhibited its antioxidative effects in a dose-dependent manner and, to some extent, outperformed vitamin C. In vivo experiments revealed that PN-CeO_2 could alleviate skin lesions through general observation and tissue Hematoxylin and Eosin staining, reduce mast cell and macrophage infiltrations, decrease scratching times, spleen indexes, and serum IgE levels. The therapeutic effect of PN-CeO_2 on AD mice was associated with the downregulation of tissue ROS levels and the activation of the antioxidant molecule Nrf2. Furthermore, PN-CeO_2 demonstrated excellent biocompatibility. Our research offers an antioxidative stress approach to AD treatment.

A Catechol Isoquinoline Salsolinol Induces Apoptosis of Human Liver Cancer Cells

Jeong-Hwa Woo[1], Hyun-Jeong Oh[2], Hong-Kyung Yang[1], Mi-Young Jeong[1], Chan-Mi, Park[2], Seah Park[2], Young-Joon Surh[3], Hye-Kyung Na* [1,2,4]

[1]Basic Science Research Institute, Sungshin Women's University, [2]Departmet of Future Applied Sciences, College of Natural Sciences, Sungshin Women's University, [3]College of Pharmacy, Seoul National University, Seoul 08826, [4]Department of Food Science & Biotechnology, College of Knowledge-Based Services Engineering, Sungshin Women's University, Seoul 01133, South Korea

**Correspondence email: jhwoo926@gmail.com*

Abstract

Liver cancer is one of the most common malignancies and a leading cause of death worldwide. However, it is still very difficult to treat and prevent liver cancer. A catechol tetrahydroisoquinoline, salsolinol (SAL) is present in our daily diets, such as mushrooms, bananas, etc. It is also endogenously generated by the condensation of dopamine with acetaldehyde. In the present study, we found that SAL inhibited the growth and colony forming ability of human hepatic carcinoma SK-Hep1 cells. The phosphorylation at Tyr 705 of signal transducer and activator of transcription factor 3 (STAT3) and its dimerization, nuclear translocation, and transcriptional activity were inhibited by SAL. The expression of cyclin D1, the major target proteins of STAT3, was suppressed, whereas the expression of cell cycle regulator p21 and its upstream regulator p53 was enhanced by SAL. p53 regulates expression of genes involved in apoptosis. SAL induced intrinsic apoptotic signaling by enhancing Bax expression and proteolytic cleavage of caspase-9/3/7 and PARP. The proportions of cell population in the subG0/G1 fraction and TUNEL positive apoptotic cells were increased by SAL. Inhibition of mitochondrial STAT3 phosphorylation (Ser727) has been associated with induction of apoptosis. SAL inhibited the phosphorylation of STAT3 (Ser727) and induced disruption of mitochondria membrane potential, which led to the downregulation of cytochrome *c* in the mitochondria fraction. A general antioxidant *N*-acetyl cysteine (NAC) attenuated suppression of STAT3 at Tyr and Ser residues and blocked the phosphorylation of STAT1 (Tyr 701) and cell death as well as generation of reactive oxygen species induced by SAL. Moreover, SAL inhibited direct interaction between Annexin A2 and STAT3 (Ser727), thereby suppressing phosphorylation of STAT3 (Ser727). Furthermore, intraperitoneal injection of SAL significantly delayed the growth of tumor and reduced the tumor volume in a SK-Hep1 xenograft mouse model. Taken together, SAL regulates STAT1/3 signaling, thereby inducing apoptosis in SK-Hep1 cells, which may account for its anti-carcinogenic activity in liver cancer.

Key Words: Salsolinol, STAT3, STAT1, Liver cancer, Apoptosis

Acute Sleep Deprivation Induces Liver Damage and Protective Effects of Chalcone Analogue TAK

Yifang Wang[1]（王一方）, Yachong Hu[1], Pengxiao Wang[1], Ranrui Hu[1], Tiantian Zhang[1], Lerong Chen[1], Jiankang Liu[1,3], Mami Noda[4,5], Jiangang Long[1]*, Yunhua Peng[1]*

1. *Center for Mitochondrial Biology and Medicine, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, Shaanxi 710049, China*
2. *School of Health and Life Science, University of Health and Rehabilitation Sciences, Qingdao, Shandong 266071, China*
3. *Laboratory of Pathophysiology, Graduate School of Pharmaceutical Sciences, Kyushu University, 3-1-1 Maidashi Higashi-ku, Fukuoka, 812-8582, Japan*
4. *RUDN University, 6 Miklukho-Maklaya St, Moscow, 117198, Russian Federation, Miklukho-Maklaya str.6*

**Correspondence email: 1131218759@qq.com*

Abstract

The prevalence of sleep deprivation (SD) is increasing globally. Previous studies mainly showed impaired body physiology as well as pathology and dysfunctions in the central nervous system. However, little is known to hepatic dysfunctions in SD studies, despite vital roles liver play in metabolism and immune response. Hepatic dysfunction is a sign of irreversible hepatic damage, characterized by metabolic disorders and increased oxidative stress. Therefore, early detection and intervention of liver dysfunction are crucial for SD-induced peripheral and central disorders. TAK, a newly developed chalcone analogue and an agent against oxidative stress, may have therapeutic potential in mitigating hepatic damage. In this study, we aim to explore the hepatic metabolic and inflammatory alterations induced by acute sleep deprivation (ASD), and to test the potential protective effects of TAK administration. Modified multi-platform method was used to prepare animal models of 72 h ASD in rats. TAK (50 mg/kg/day) was irrigated 1 week before experiment, and last 3 days during the experiment. Blood biochemistry, tissue staining, qPCR, inflammation factor gene expressions, and western blotting were performed to assess hepatic damage. ASD-induced the increases of inflammatory cytokines IL1 and TNF-α in both serum and liver tissue. PAS and Oil-rad staining of liver tissues showed glycogen decrease and lipid accumulation in the liver of rats. Moreover, ASD unbalanced M1 and M2 states of Kupffer cells (KCs). Hepatic portal areas showed SD-triggered fibrosis as revealed by Masson and Sirius red staining. TAK could significantly alleviated ASD-induced hepatic metabolic disorder, inflammation and fibrosis. ASD induces hepatic damage including metabolic reprogramming, inflammation and fibrosis while TAK could effectively reduce the ASD-induced hepatic damage.

Key Words: Sleep deprivation；liver damage；chalcone analogue TAK

Assessing Myriocin and N-Acetyl Cysteine on Age-Related Hearing Loss and disruption of Advanced Glycation End Products in mice

Lin Cheng[2]（程琳）, Zhiyi Liu[1], Ke Liu[1]*

[1]*Key Laboratory of Bio-Resources and Eco-Environment of Ministry of Education, College of Life Science, Sichuan University, 610065, Chengdu China*

[2]*State Key Laboratory of Biotherapy, Sichuan University, 610041, Chengdu China*

**Correspondence email: kliu@scu.edu.cn*

Abstract

Age-related hearing loss (ARHL) is the most prevalent sensory disorder among the elderly associated with mitochondrial dysfunction and oxidative stress. Myriocin, a specific sphingolipid synthesis inhibitor derived from entomopathogenic fungi, has potential for managing redox homeostasis. Advanced glycation end products (AGEs), formed through Maillard reaction, have been linked to hearing impairment. N-acetyl cysteine (NAC), an antioxidant derived from L-cysteine, is known to mitigate ARHL.

Our preliminary research indicates that myriocin can enhance cellular protection by modulating mitochondrial redox balance. To further investigate, we conducted an experiment using C57BL/6J mouse model, divided into eight treatment groups with myriocin, AGEs, and NAC. We assessed mouse weight and food intake weekly, and auditory brainstem response (ABR) monthly to evaluate the effects of these treatments on aging and AGEs-induced weight, diet and hearing changes.

After five months, our data revealed no significant impact of myriocin, AGEs, and NAC on mouse weight and food consumption. Control and myriocin-treated mice exhibited significant hearing loss at all tested frequencies with advancing age. However, NAC-treated and myriocin-NAC double-treated group did not show significant hearing loss at mid and low frequencies. Notably, the myriocin-NAC combination group demonstrated slightly better hearing at 4k and 5.6kHz compared to the NAC-only group at seven months. AGEs did not significantly affect hearing levels in this study.

Overall, while treatments with AGEs, myriocin, and NAC did not influence weight and diet, NAC exhibited protective effects against ARHL at mid and low frequencies. Additionally, the myriocin-NAC combination may offer synergistic benefits at low frequencies. Future research will focus on biochemical analyses of each group and further explore the molecular mechanisms underlying NAC and myriocin's therapeutic effects on hearing.

Key Words: Age-related hearing loss, Myriocin, Advanced glycation end products, N-acetyl cysteine

Characterization of a polysaccharide from Amauroderma rugosum and its proangiogenic activities in vitro and in vivo

Xin Nie[a,b,1]（聂欣）, Jingjing Li[b,f,1,*], Nan Xu[a], Yulin He[b], Jinming Zhang[c], Simon Ming-Yuen Lee[e,f,*]

[a] *State Key Laboratory of Quality Research in Chinese Medicine and Institute of Chinese Medical Sciences, University of Macau, Macao SAR, China;*

[b] *Department of Rehabilitation Sciences, Faculty of Health and Social Sciences, Hong Kong Polytechnic University, Hong Kong SAR, China;*

[c] *State Key Laboratory of Southwestern Chinese Medicine Resources, School of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu, China;*

[d] *Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China;*

[e] *Department of Food Science and Nutrition, Faculty of Science, Hong Kong Polytechnic University, Hong Kong, China;*

[f] *The Research Centre for Chinese Medicine Innovation, Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China*

[1] *Xin Nie and Jingjing Li contribute equally.*

**Correspondence email: kim07.li@polyu.edu.hk*

Abstract

Amauroderma rugosum (AR), also known as “Blood Lingzhi” in Chinese, is a basidiomycete belonging to the Ganodermataceae family. Four polysaccharide fractions were systematically isolated and purified from AR. Subsequently, their compositions were examined and analyzed via high-performance gel permeation chromatography (HPGPC), analysis of the monosaccharide composition, Fourier-transform infrared spectroscopy (FT-IR), and ^{1}H nuclear magnetic resonance (NMR). The zebrafish model was then used to screen for proangiogenic activities of polysaccharides by inducing vascular insufficiency with VEGF receptor tyrosine kinase inhibitor II (VRI). The third fraction of AR polysaccharides (PAR-3) demonstrated the most pronounced proangiogenic effects, effectively ameliorating VRI-induced intersegmental vessel deficiency in zebrafish. Concurrently, the mRNA expression levels of vascular endothelial growth factor (VEGF)-A and VEGF receptors were upregulated by PAR-3. Moreover, the proliferation, migration, invasion, and tube formation of human umbilical vein endothelial cells (HUVECs) were also stimulated by PAR-3, consistently demonstrating that PAR-3 possesses favorable proangiogenic properties. The activation of the Akt, ERK1/2, p38 MAPK, and FAK was most likely the underlying mechanism. In conclusion, this study establishes that PAR-3 isolated from *Amauroderma rugosum* exhibits potential as a bioresource for promoting angiogenesis.

Key Words: *Amauroderma rugosum*; polysaccharides; proangiogenesis

Co-Treatments of Gardeniae Fructus and Silymarin Ameliorates Excessive Oxidative Stress-Driven Liver Fibrosis by Regulation of Hepatic Sirtuin 1 Activities Using Thioacetamide-Induced Mice Model

Jin A Lee [1 2], Mi-Rae Shin [1], JeongWon Choi [1], MinJu Kim [1], Hae-Jin Park [3], Seong-Soo Roh [1]

1: Department of Herbology, College of Korean Medicine, Daegu Haany University, Daegu 42158, Republic of Korea.
2: Research Center for Herbal Convergence on Liver Disease, Daegu Haany University, Gyeongsan 38610, Republic of Korea.
3: Bio Convergence Testing Center, Daegu Haany University, Gyeongsan 38610, Republic of Korea.

**Correspondence email:*

Abstract

Gardeniae Fructus (GF, the dried ripe fruits of Gardenia jasminoides Ellis) has traditionally been used to treat various diseases in East Asian countries, such as liver disease. Silymarin is a well-known medicine used to treat numerous liver diseases globally. The present study was purposed to evaluate the synergistic effects of GF and silymarin on the thioacetamide (TAA)-induced liver fibrosis of a mouse model. Mice were orally administered with distilled water, GF (100 mg/kg, GF 100), silymarin (100 mg/kg, Sily 100), and GF and silymarin mixtures (50 and 100 mg/kg, GS 50 and 100). The GS group showed remarkable amelioration of liver injury in the serum levels and histopathology by observing the inflamed cell infiltrations and decreases in necrotic bodies through the liver tissue. TAA caused liver tissue oxidation, which was evidenced by the abnormal statuses of lipid peroxidation and deteriorations in the total glutathione in the hepatic protein levels; moreover, the immunohistochemistry supported the increases in the positive signals against 4-hydroxyneal and 8-OHdG through the liver tissue. These alterations corresponded well to hepatic inflammation by an increase in F4/80 positive cells and increases in pro-inflammatory cytokines in the hepatic protein levels; however, administration with GS, especially the high dose group, not only remarkably reduced oxidative stress and DNA damage in the liver cells but also considerably diminished pro-inflammatory cytokines, which were driven by Kupffer cell activations, as compared with each of the single treatment groups. The pharmacological properties of GS prolonged liver fibrosis by the amelioration of hepatic stellate cells' (HSCs') activation that is dominantly expressed by huge extracellular matrix (ECM) molecules including α-smooth muscle actin, and collagen type1 and 3, respectively. We further figured out that GS ameliorated HSCs activated by the regulation of Sirtuin 1 (Sirt1) activities in the hepatic protein levels, and this finding excellently reenacted the transforming growth factor-β-treated LX-2-cells-induced cell death signals depending on the Sirt1 activities. Future studies need to reveal the pharmacological roles of GS on the specific cell types during the liver fibrosis condition.

Key Words: Gardeniae Fructus; Sirtuin 1; liver fibrosis; oxidative stress; silymarin.

Daphnetin ameliorates hepatic steatosis by suppressing peroxisome proliferator-activated receptor gamma (PPARG) in ob/ob mice

Zhen Wang（王珍）, Le Shi, Jiangang Long*

Center for Mitochondrial Biology and Medicine, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science, Xi'an Jiaotong University. 710049. 28 West Xianning Road, Xi'an, China.

**Correspondence email: 1097216506@qq.com.*

Abstract

Non-alcoholic fatty liver disease (NAFLD) is the predominant metabolic liver disorder and currently lacks effective and safe pharmaceutical interventions. Daphnetin (DA), a natural coumarin derivative with anti-inflammatory and antioxidant activities, is a promising agent for NAFLD treatment. In this study, we evaluated the effects and mechanisms of DA on hepatic lipid metabolism in ob/ob mice. Our results showed that DA effectively ameliorates glucose metabolism and hepatic lipid accumulation in ob/ob mice. Metabolomics and RNA sequencing (RNA-seq), combined with GEO data analysis, suggest that DA primarily modulates the peroxisome proliferator-activated receptor gamma (PPARG) pathway, as validated *in vivo* in ob/ob mice. Mechanistically, DA selectively targets PPARG in hepatic cells by inhibiting *PPARG* promoter activity and downregulating its expression, resulting in decreased transcription of downstream lipid metabolism-related genes, including fatty acid binding protein 4 (*Fabp4*), cluster of differentiation 36 (*Cd36*), and fatty acid synthase *(Fasn)*. This effect was abolished in *PPARG*-deficient HepG2 cells subjected to palmitic acid (PA) insult. Our findings provide evidence that DA acts as a selective suppressor of hepatic PPARG, suggesting an attractive strategy by targeting PPARG for the prevention of hepatic steatosis.

Emodin, a major component of Cassia seed extract, exhibits potent anti-inflammatory effects in vitro and in vivo

Kwanhwan Wi[1], Young-Gwon Kim[1], Sun-Young Hwang[1], Mee-Hyun Lee[1*]

[1]*College of Korean Medicine, dongshin University, Naju, Jeonnam 58245, Republic of Korea*

**Correspondence email: hwan1513@naver.com*

Abstract

Rerearch purpose : Inflammatory bowel disease (IBD), primarily represented by ulcerative colitis (UC), is associated with significant pain and a reduced quality of life. *Cassia* seed extracts have been used for the treatment of cataracts, neurodegenerative diseases, and metabolic disorders. The purpose of this study was to investigate the effects of emodin, a major component of *Cassia* seed extracts, on 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced cell transformation and dextran sulfate sodium (DSS)-induced inflammation *in vitro* and *in vivo*.

Methods : The cytotoxicity of emodin were evaluated using the MTT assay, and the effects of emodin on TPA-induced cell transformation were assessed using the soft agar assay. Acute colitis was induced in mice by administering 3% DSS in drinking water for one week, simultaneously emodin was given by intragastric administration, then monitored disease activity index (DAI). The colon tissues were paraffin-embedded by autoprocessor and cut into sections then conducted H&E and IHC staining.

Results : In this research, emodin did not exhibit significant cytotoxicity. Furthermore, emodin effectively inhibited TPA-induced colony formation and growth in a dose-dependent manner. Additionally, in a mouse model of DSS-induced colitis, emodin treatment significantly ameliorated symptoms of colitis, as indicated by reduced weight loss, decreased colon shortening, and lower DAI scores compared to the DSS group. Histopathological analysis showed that emodin effectively decreased mucosal damage. Immunohistochemical (IHC) analysis revealed that emodin substantially reduced the expression of Ki-67 and COX2 in the colonic tissues, suggesting a significant decrease in cellular proliferation and inflammation.

Conclusion : This study demonstrates that emodin effectively inhibits cell transformation induced by TPA and exhibits significant anti-inflammatory effects in the treatment of DSS-induced colitis. These findings indicate that emodin could be a promising therapeutic agent for colitis treatment. Ongoing studies are needed to fully understand the molecular mechanisms of emodin.

Key Words: Emodin, Cassia seed extracts, Colitis, Dextran sulfate sodium

Exploring the Mechanisms of Action of Active Constituents in Schisandrae Fructus for the Management of Diabetic Cardiomyopathy

Daozheng Fang[1,2], Qixiang Shang[1,2], Quanrun He[1,2], Xinhang Li[1,2], Haimeng Li[1,2], Xinyue Li[1,2], Zhihao Liu[1,2], Yong Zhu[1,2]and Jihang Chen[1,2*](陈吉航)

1.School of Medicine, The Chinese University of Hong Kong, Shenzhen, China;

2.The Chinese University of Hong Kong, Shenzhen Futian Biomedical Innovation R&D Center, Shenzhen, China.

**Correspondence email: chenjihang@cuhk.edu.cn*

Abstract

Diabetes mellitus is a prevalent chronic metabolic disorder with a high incidence rate. It is estimated that by the year 2030, the global prevalence of diabetes mellitus will rise to 578 million individuals. Prolonged elevated blood glucose levels can detrimentally impact various organs in patients, leading to a range of diabetic complications. Diabetic cardiomyopathy remains a major cause of death, accounting for approximately 50-80% of diabetes-related fatalities.

Schisandra chinensis, a member of Schisandraceae family, is a common woody plant native to China, Korea, and Japan. Recent studies have shown that Schisandrin A and Schisandrin B derived from Schisandrae Fructus demonstrated protective effects against diabetic cardiomyopathy. Therefore, elucidating the mechanisms of action of the main components of Schisandra chinensis holds significant economic and social value.

Through different in vivo and in vitro models, we have observed that the alleviation of diabetic cardiomyopathy by Schisandrin A and Schisandrin B relies on a comprehensive network of multi-organ cooperation. This network demonstrates protective abilities not only towards the heart and pancreas but also exhibits certain clearance capabilities in major lipid and glycogen-storing organs such as the liver and kidney. Moreover, through transcriptomics analysis, we have discovered that Schisandrin A and Schisandrin B exhibit distinct mechanisms of action in the two main subtypes of diabetes. In type 1 diabetes, they exert strong regulatory effects on the complement system, inhibiting key members of this pathway such as C3, C3a, and C5a. However, in type 2 diabetes, the focus shifts to mitochondrial oxidative phosphorylation. We aim to further explore the respective main targets within the frameworks of type 1 and type 2 diabetic cardiomyopathy. Although a member of the heat shock protein family, Grp94, has been previously identified as one of the main targets previously, a comprehensive understanding of the multi-organ cooperative network of Schisandrin A and Schisandrin B undoubtedly requires support from additional targets.

Key Words: Diabetic cardiomyopathy, Schisandrae Fructus, Mitochondrial function, drug target discovery

Ferulic acid as a potent natural antioxidant: mechanisms and applications in animal health and production

Yongquan Han

Guangzhou Cohoo Biotechnology Co., Ltd.

**Correspondence email:*

Abstract

Oxidative stress and inflammation are major biological factors influencing animal health and growth performance. Ferulic acid (FA), a natural antioxidant abundant in various plants and agricultural by-products, has shown promising potential in maintaining redox homeostasis and coordinating non-specific immune responses in animals. This study aims to elucidate the mechanisms of FA's antioxidant and anti-inflammatory activities and its applications in promoting animal growth and health.

We investigated the effects of dietary FA supplementation on growth performance, antioxidant capacity, and immune function in oriental river prawn (Macrobrachium nipponense) challenged with oxidized fish oil. Shrimps were fed diets containing 0, 160, or 320 mg/kg FA for 10 weeks. Results showed that 160 mg/kg FA significantly improved growth rate, feed efficiency, and muscle percentage compared to the control group. FA supplementation also enhanced hepatopancreatic antioxidant enzyme activities, reduced lipid peroxidation, and modulated the expression of immune-related genes (Toll-Dorsal and IMD-Relish pathways).

Furthermore, we explored the molecular mechanisms underlying FA's antioxidant and anti-inflammatory activities. FA exhibited strong free radical scavenging and chain-breaking capabilities due to its unique chemical structure. It also regulated key signaling pathways (NF-κB, MAPKs, and AP-1) to inhibit the production of pro-inflammatory mediators and cytokines.

In conclusion, our findings demonstrate that FA, as a potent natural antioxidant, can effectively alleviate oxidative stress, maintain redox balance, and enhance immune function in animals. Its application in animal production shows great promise in promoting growth, improving feed utilization, and preventing diseases. This study provides valuable insights into the mechanisms and potential of using natural antioxidants like FA in precision animal health management and sustainable production.

Key Words:

oxidative stress, ferulic acid, antioxidant, Macrobrachium nipponense, lipid metabolism

Gaudichaudione H ameliorates liver fibrosis and inflammation by targeting NRF2 signaling pathway

Mengjiao Shi（石梦姣），Ying Guo ,Jiayi Xu, Xinyan Li, Pengfei Liu

National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University

**Correspondence email: shimengjiao_xj@xjtu.edu.cn*

Abstract

Gaudichaudione H (GH) is a natural small molecular compound isolated from Garcinia oligantha Merr. (Clusiaceae). Being an uncommon rare caged polyprenylated xanthone, the potential pharmacological functions of GH remain to be fully elucidated currently. In this study, we primarily focused on identifying potential bioavailable targets and elucidating related therapeutic actions. Herein, the network pharmacology analysis, metabolomics analysis and genome-wide mRNA transcription assay were performed firstly to predict the major pharmacological action and potential targets of GH. To confirm the hypothesis, gene knockout model was created using CRISPR/Cas9 method. The pharmacological action of GH was evaluated in vitro and in vivo. Firstly, our results of network pharmacology analysis and omics assay indicated that GH significantly activated NRF2 signaling pathway, and the function could be associated with liver disease treatment. Then, the pharmacological action of GH was evaluated in vitro and in vivo. The treatment with GH significantly increased the protein levels of NRF2 and promoted the transcription of NRF2 downstream genes. Further analysis suggested that GH regulated NRF2 through an autophagy-mediated non-canonical mechanism. Additionally, the administration of GH effectively protected the liver from CCl4-induced liver fibrosis and inflammation, which depended on the activation of NRF2 in hepatic stellate cells and inflammatory cells respectively. Collectively, our findings underscore the potential therapeutic effect of GH on alleviating hepatic fibrosis and inflammation through the augmentation of NRF2 signaling pathway, providing a promising avenue for the treatment of liver fibrosis and inflammation in clinical settings.

Key Words: gaudichaudione H; liver fibrosis; liver inflammation; NRF2; autophagy

Neem Leaf Extract Exhibits Anti-Aging and Antioxidant Effects from Yeast to Human Cells

jinye Dang（党劲野）, Gongrui Zhang, Ke Liu*

Key Laboratory of Bio-Resources and Eco-Environment of Ministry of Education, College of Life Science, Sichuan University, 610065, Chengdu China

**Correspondence email: kliu@scu.edu.cn*

Abstract

Neem leaves have been traditionally employed in medicine for their purported longevity-enhancing properties. Despite their widespread use, the exact mechanisms behind their anti-aging benefits remain unclear. In this study, we explored the effects of neem leaf extract (NLE), derived from a 50% ethanol solution, on the chronological lifespan of *Saccharomyces cerevisiae*. Our findings indicate that NLE significantly extends chronological lifespan, enhances resistance to oxidative stress, and reduces reactive oxygen species. To identify the active compounds in NLE, we utilized LC/MS and the GNPS platform, revealing that most of the active components are flavonoids. We then constructed compound-target pharmacological networks using the STP and STITCH platforms for both S. cerevisiae and Homo sapiens. Enrichment analyses of predicted targets through GOMF and KEGG highlighted "oxidoreductase activity" as a top enriched term in both yeast and human cells, suggesting NLE's potential role in regulating oxidative stress response. RNA-seq analysis of NLE-treated yeast supported the anti-oxidative effects, with "oxidoreductase activity" and "oxidation-reduction process" being prominent in enriched GO terms. Notably, CTT1, which encodes catalase, was the most significantly upregulated gene within the "oxidoreductase activity" cluster. In a *ctt1* null mutant, the beneficial effects of NLE on oxidative stress resistance and lifespan extension were abolished. For human cells, NLE pretreatment demonstrated a decrease in reactive oxygen species levels and senescence-associated β-galactosidase activity in HeLa cells, underscoring its anti-aging and anti-oxidative effects. This study highlights the anti-aging and anti-oxidative properties of NLE and elucidates its mechanisms, offering new insights for potential phytochemical-based interventions in aging.

Key Words: *Azadirachta indica*; aging; antioxidant; catalase; *Saccharomyces cerevisiae*; chronological lifespan; network pharmacology

Saikosaponin A suppresses inflammation in DSS-induced colitis mouse model

Young-Gwon Kim[1], Kwanhwan Wi[1], Sun-Young Hwang[1], Mee-Hyun Lee[1]

[1]College of Korean Medicine, Dongshin University, Naju, Jeonnam 58245, Republic of Korea

Correspondence email: kyg1022@hanmail.net

Abstract

Research purpose: Ulcerative colitis(UC) is a major inflammatory bowel diseases (IBD) that affects millions of people worldwide and is characterized by inflammation of the colon and rectum accompanied by metabolic disorders. This study investigate the effects of Saikosaponin A on dextran sulfate sodium (DSS)-induced colitis in mice.

Methods: Mice were treated with 3% DSS in drinking water for 7 days, followed by autoclaved tap water for 3 days to induce acute colitis. Saikosaponin A was administered intragastrically during DSS treatment for 7 days. The body weight of each mouse was measured every day together with observing the fecal characteristics and hematochezia. The disease activity index (DAI) was calculated by scores including weight loss percents, stool trait and blood in stool. The colon tissues were fixed with 10% paraformaldehyde, dehydrated, and embedded in paraffin. Then, the tissues were cut into 5 m sections and stained with H&E, Alcian blue and IHC staining. The histological changes of colonic pathology were observed by optical microscopy and scored.

Results: Compared with control group, the body weight, colon length and DAI score deteriorated in the DSS group, while Saikosaponin A treatment improved upon the parameters. In addition, we found that histopathological changes by H&E staining were higher in the DSS group, but the Saikosaponin A had significantly improved. Alcian blue staining confirmed that goblet cells were decreased in DSS-treated group while significantly increased in Saikosaponin A treated group. Moreover, Saikosaponin A treatment increased MUC2 expression and decreased COX2 level in IHC staining.

Conclusion: Saikosaponin A significantly mitigated DSS-induced body weight loss and colon length shortness and colonic histological changes. These findings suggest that Saikosaponin A has the potential to be used as an agent for the treatment of intestinal inflammatory diseases.

Key Words: Saikosaponin A, Ulcerative colitis, Dextran sulfate sodium

Salsolinol Alleviates Tumor Formation and Anxiety Like Behaviors in the Diethyl Nitrosamine-induced Hepatocarcinogenesis in Mice

Chan-Mi Park[1], Jeong-Hwa Woo[2], Hyun-Jeong Oh[1], Seah Park[1], HongKyung Yang[2], Hoon Ryu[3], Young-Joon Surh[4], Hye-Kyung Na[1,2,5*]

[1]Department of Future Applied Sciences, College of Natural Sciences, Sungshin Women's University, Seoul 01133, [2]Basic Science Research Institute, Sungshin Women's University, [3]Brain Science Institute, Korea Institute of Science and Technology, Seoul 02792, [4]College of Pharmacy, Seoul National University, Seoul 08826, [5]Department of Food Science and Biotechnology, College of Knowledge-Based Services Engineering, Sungshin Women's University, Seoul 01133, Republic of Korea

**Correspondence email: chanmi217@gmail.com*

Abstract

Salsolinol (SAL) is an endogenous catechol isoquinoline generated by condensation of dop amine with acetaldehyde. It is also present in our daily diets such as bananas, mushroom s and lettuce. In our previous research, SAL inhibited the growth of liver cancer cells by regulating the STAT1/3 signaling pathway. In this study, we found that SAL inhibited d iethyl nitrosamine (DEN)-induced murine hepatocarcinogenesis without affecting body weig ht change. Additionally, the plasma level of -fetoprotein, a clinical biomarker of liver c ancer, was reduced in the mice injected with SAL. The expression of proliferative marker s PCNA, Ki-67 and pSTAT3(Y705) were also down-regulated in the tumor tissue of SAL -treated mice. Considering the structural similarity between an *N*-methylated metabolite of SAL and the neurotoxin, 1-methyl-4-phenylpyridinum ion, we performed an open field tes t to determine the effects of SAL on brain function during DEN-induced murine hepatoca rcinogenesis. Notably, anxiety-like behavior by center frequency was observed in the mice treated with DEN, which was substantially decreased in the mice injected with SAL wit hout affecting the locomotive activities. Moreover, the expression of dopamine- and cAM P-regulated phosphoprotein-32 in the nucleus accumbens and tyrosine hydroxylase, a key enzyme for generation of dopamine in substantia nigra, was enhanced in the brain of the SAL-injected mice in the DEN-induced liver carcinogenesis. To investigate what might c ause brain disorders in the cancer state and how SAL could restore the brain function, w e measured the levels of TNF- and IL-6 in murine hippocampal neuronal HT-22 cells t reated with SK-Hep1 conditioned media (CM). The levels of these pro-inflammatory cytok ines were elevated in HT-22 cells treated with SK-Hep1-CM, which was decreased in the HT-22 cells treated with SK-Hep1-CM treated with SAL (SAL-CM). In addition, SAL-C M reduced generation of reactive oxygen species and the oxidative stress marker, 4-hydro xynonenal in HT-22 cells. Furthermore, the mitochondria membrane potential was also res tored in the HT-22 cells treated with SAL-CM. These findings suggest potential therapeuti c benefits of SAL in the management of liver cancer development.

Key Words: Salsolinol, DEN-induced liver carcinogenesis, Anti-cancer, Neuroprotection, ROS.

获硕贝肯

获硕贝肯科研服务

获硕贝肯（Tissue And Bank)是一家专注于免疫医学科学与科技创新产业化的机构。公司在免疫医学科学研究、免疫组织储存、免疫医学特检、免疫治疗评估、免疫诊断试剂等免疫医学领域进行全方位的科学研究与创新产业化。

获硕贝肯基于免疫平台与分子生物学平台、质谱平台，围绕HLA，提供多维度的科研服务，包括免疫医学特色项目、微生物组学、代谢组学、蛋白组学以及其他组学产品与个性化科研服务。

免疫组

免疫组是研究免疫相关的全套分子库，它们的作用靶分子及其功能。包括实体肿瘤HLA-loss检测、免疫组库、免疫肽组-肿瘤抗原肽，四聚体技术等产品。

微生物组

扩增子测序和宏基因组测序是两种常用的方法。扩增子测序获得环境样本中的微生物群落结构、进化关系以及微生物与环境相关性等信息。宏基因组主要研究微生物种群结构、基因功能、微生物之间的相互协作关系以及微生物与环境之间的关系。

代谢组

代谢组学主要目标是定性定量地研究生命体对外界刺激、生理病理变化以及基因突变而产生的体内代谢物水平的多元动态反应，研究对象大多是相对分子质量≤1000 Da的小分子物质，如有机酸、氨基酸、核苷酸、糖、脂质、维生素等。

单细胞转录组

在单细胞水平直接分析基因表达，并在单细胞水平分析细胞内群体异质性、定义细胞类型、细胞状态和细胞的动态转变，除了识别新的细胞亚型和稀有细胞群外，单细胞测序技术还能更好地理解转录动力学和基因调控关系。

蛋白组

蛋白质组学是指在大规模水平上探索蛋白质的特征，包括蛋白质的表达水平，翻译后的修饰，蛋白与蛋白相互作用等，由此获得在蛋白质水平上的关于疾病发生，细胞代谢等过程的整体而全面的认识。

上海获硕贝肯生物科技有限公司

SHANGHAI TISSUEBANK BIOTECH Co.,Ltd

荻硕贝肯

产品目录

免疫组

HLA-LOSS
免疫组库
抗原肽
四聚体

微生物组

扩增子测序
宏基因组测序

单细胞转录组

单细胞3'转录组测序
单细胞5'转录组+免疫组库测序
单细胞全序列转录组测序
空间转录组测序

蛋白组

Astral-DIA 中度血液蛋白组学
Astral-DIA 深度血液蛋白组学
Astral-DIA 高深度血液蛋白组学
磷酸化修饰蛋白组

代谢组

非靶向代谢组学
靶向代谢组学 (氨基酸，短链脂肪酸等)
高通量靶向代谢组学
脂质组学
代谢流

多组学

蛋白组+代谢组
代谢组+微生物组
转录组+蛋白组
单细胞转录组+空间转录组

服务流程

联系我们

微信公众号　　业务咨询号

www.catb.org.cn
400-968-0001
imsspm@catb.org.cn
上海市浦东新区康新公路3377号9-10号楼

拨打咨询电话或者关注微信公众号获取更多产品详情和案例分享。

Publish with Elsevier's

Redox Journals

ELSEVIER

ABclonal Technology® | 爱博泰克

氧化还原研究精选SMab®重组兔单抗

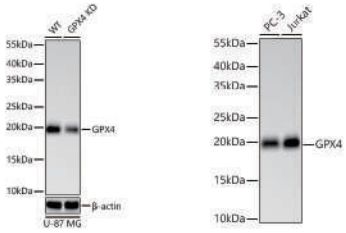
ABclonal基于自有知识产权的SMab®单B细胞抗体开发平台研发生产的重组兔单抗，突破了传统鼠单抗的局限，展现出更卓越的性能。SMab®重组兔单抗具有高特异性、高亲和力、高灵敏度、广泛的多样性、批次间的高一致性等核心优势。目前，SMab®重组兔单抗现货产品覆盖自由基生成、抗氧化系统、GSH和NADPH生成相关的核心靶点。

精选产品

GPX4 | KO/KD Validated | 重组 兔单抗

A11243 [KD Validated] GPX4 Rabbit mAb

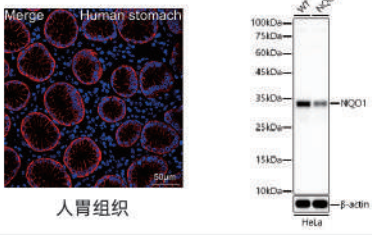
应用: IF/ICC, WB, ELISA
物种: H, M, R
文献引用(68篇)



NQO1 | KO/KD Validated | 重组 兔单抗

A19586 [KD Validated] NQO1 Rabbit mAb

应用: IF/ICC, WB, ELISA
物种: H, M, R
文献引用(44篇)

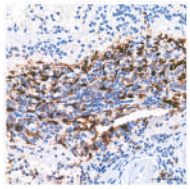


人胃组织

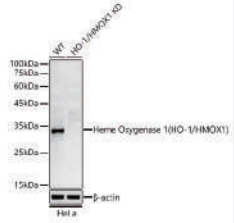
HO-1 | KO/KD Validated | 重组 兔单抗

A19062 [KD Validated] Heme Oxygenase 1 (HO-1/HMOX1) Rabbit mAb

应用: IF/ICC, IHC-P, WB, ELISA
物种: H, M, R
文献引用(42篇)



人脾脏组织



氧化还原研究精选产品列表

Target	Cat. No.	Product Name	Application	Reactivity
NADPH oxidase (NOX)	A19701	NOX2/gp91phox Rabbit mAb	WB, ELISA	H, M, R
	A3703	NOXA2/p67phox Rabbit mAb	WB, IHC-P, ELISA	M, R
	A22149	NADPH oxidase 4 (NOX4) Rabbit mAb	WB, IF/ICC, ELISA	H, M, R
Nitric oxide synthase (NOS)	A3774	iNOS Rabbit mAb	WB, IF/ICC, ELISA	M, R
	A20985	eNOS Rabbit mAb	WB, IHC-P, ELISA	H, M, R
Cycloxygenase (COX)	A3560	COX2/PTGS2 Rabbit mAb	WB, IHC-P, ELISA	H, M, R
Lipoxygenase	A2877	ALOX5 Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
	A22908	ALOX15 Rabbit mAb	WB, IHC-P , ELISA	H, M, R
Xanthine oxidase (XOR)	A9022	Xanthine Oxidase (XDH) Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
SOD2	A19576	[KO Validated] SOD2 Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
HO-1	A19062	[KD Validated] Heme Oxygenase 1 (HO-1/HMOX1) Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
GPX4	A25009	[KD Validated] GPX4 Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
	A11243	[KD Validated] GPX4 Rabbit mAb	WB, IF/ICC, ELISA	H, M, R
Thioredoxin 1	A4024	Thioredoxin 1 (Trx1/TXN) Rabbit mAb	WB, IHC-P, ELISA	H, M, R
Thioredoxin 2	A4424	Thioredoxin 2 (Trx2/TXN2) Rabbit mAb	WB, IF/ICC, ELISA	H, M, R
NQO1	A19586	[KD Validated] NQO1 Rabbit mAb	WB, IF/ICC, ELISA	H, M, R
PRDX3	A2398	Peroxiredoxin 3 (PRDX3) Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M
PRDX4	A9131	Peroxiredoxin 4 (PRDX4) Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
NRF2	A25327	[KO Validated] NRF2 Rabbit mAb	WB, IHC-P, IF/ICC, ELISA	H, M, R
	AP1133	Phospho-NRF2-S40 Rabbit mAb	WB, IHC-P, ELISA	H, M, R

400-999-6126
cn.market@abclonal.com
官方微信公众号

上海碧云天生物技术股份有限公司
Beyotime Biotech Inc

碧云天创办于2001年。20余年来专注于自主研发和生产。公司现有在售产品**5万**余种，拥有核酸相关、多肽与蛋白、细胞相关、信号转导、抗体、抑制剂激活剂、常用试剂、耗材、仪器、技术服务等全面丰富的产品线，可提供分子、蛋白、细胞、动物实验相关的全套产品及服务解决方案。

截止2024年8月，已有累计超过**200000篇**注明使用碧云天产品的研究论文发表在包括Cell、Nature、Science等国际高水平学术期刊。Beyotime品牌2023年度文献引用率国内领先，全球**20强**。

Founded in 2001, Beyotime Biotech Inc is committed to technology development and product manufacturing. We offer over **50,000** products for life science research, including reagents, kits, lab consumables, equipment, and customized services.

To date, our products had been cited in more than **200,000** peer-reviewed research articles, many of which are published in top-tier journals such as Cell, Nature, Science, and their sub-journals. **The annual citation rate of Beyotime products in 2023 ranked among the top 20 in the world.**

氧化应激检测

Oxidative Stress Detection

涵盖过氧化氢、超氧化物阴离子、单线态氧、线粒体超氧化物、NO、脂质氧化/过氧化、SOD、Catalase、NAD/NADH、NADP/NADPH、GSH/GSSG、GR、GPx、T-AOC、巯基、XOD、等多种关键指标！灵敏度高，检测快速、使用便捷！

Rapid and convenient detection of various key oxidative stress indicators such as hydrogen peroxide, superoxide anion, singlet oxygen, mitochondrial superoxide, NO, lipid oxidation/peroxidation, SOD, catalase, NAD/NADH, NADP/NADPH, GSH/GSSG, GR, GPx, T-AOC, thiols, and XOD, with high sensitivity.

代谢小分子检测

Secondary Metabolite Detection

提供乳酸/乳酸脱氢酶、黄嘌呤/黄嘌呤氧化酶、脂代谢相关、TCA相关等常见代谢指标，灵敏度高，特异性强，产品丰富，方法灵活！

Various secondary metabolism-related assays of lactate/lactate dehydrogenase, xanthine/xanthine oxidase, lipid metabolism, and TCA cycles, etc, with high sensitivity and strong specificity.

一站式核酸、蛋白、细胞解决方案

One-stop Solutions for Nucleic Acid, Protein, and Cell Biology Related Research

提供细胞活性检测、细胞转染、细胞株/培养液/血清、细胞培养添加剂、报告基因检测、核酸抽提纯化、基因检测、质粒、引物、Western Blot、蛋白表达纯化、蛋白检测、重组蛋白、抗体、生化试剂、抑制剂及激活剂等全套产品，自主研发，品质保证！

Comprehensive products covering cell viability assays, cell transfection, cell lines/culture media/sera, cell culture supplements, reporter gene assays, nucleic acid extraction and purification, genetic testing, plasmids, primers, Western blot, protein expression and purification, protein detection, recombinant proteins, antibodies, biochemical reagents, inhibitors, and activators. All products are self-developed and come with quality assurance.

技术服务

Customized Services

WB检测、双萤光素酶报告基因检测、流式细胞检测、CRISPR/Cas9基因敲除细胞系定制、Co-IP等近50余种技术服务项目，一站式服务，品质保证，提供完整实验报告和所有原始数据，真实可靠！

Over 50 types of services covering Western blot, dual-luciferase assay, flow cytometric analysis, gene knockout by CRISPR/Cas9, and Co-IP, etc, providing complete experimental reports and original data.

欢迎您来B9展位进一步了解交流！ Warm welcome to booth B9!

www.beyotime.com

ALL ABOUT STRESS AND ANTI-STRESS

中国科技期刊卓越行动计划高起点新刊

STRESS BIOLOGY

A SPRINGER NATURE partner journal

OPEN ACCESS

Home Page WeChat

FREE

Stress Biology aims to be a leading international academic journal, dedicated to promoting a systems-level understanding of stress biology by publishing cutting-edge research and systematic reviews on the broadest aspects of stress biology. Stress Biology publishes original high-quality research of all aspects of stress Biology, including but not limited to work that:

(1) provides fundamental insights into the understanding of responses of plants, microorganisms and animals to abiotic and biotic stresses;
(2) elucidates the mechanisms underlying the adaptation and resistance of plants, microorganisms and animals to biotic and abiotic stresses; and
(3) uses biotechnological and other strategies to improve the resistance of plants, microorganisms and animals to abiotic and biotic stresses.

EDITORIAL BOARD

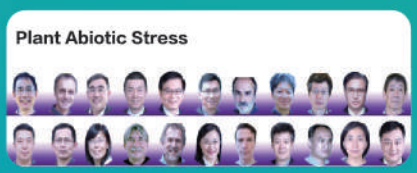
Hua-Zhong Shi
Associate Editor-in-Chief
Professor of Texas Tech University, USA

Jin-Rong Xu
Associate Editor-in-Chief
Professor of Purdue University, USA

Jian-Kang Zhu
Editor-in-Chief
Member of the US National Academy of Sciences

Zhen-Sheng Kang
Editor-in-Chief
Academician of the Chinese Academy of Engineering

60 Editors **11** Countries **48%** Overseas **43** AVG *h*-index



ARTICLE TYPES

★ Original Article
★ Review
★ Short Communication
★ Highlights
★ Letter to the Editors
★ Editorial

HOT TOPICS

★ Pathology
★ Stress resistance breeding
★ Stress sensing and signaling
★ Redox biology
★ Plant-microbe interaction
★ Virus-fungi interaction
★ Immunity
★ Epigenetics
★ Gene editing

JOURNAL METRICS

Indexed
ESCI,PMC,Scopus,DOAJ, Google Scholar,CNKI

6 days
Submission to **first decision(2023)**

30 days
acceptance to **online publication (2023)**

249,298
Downloads (2023)

43%
acceptance (2023)

11 countries of
authors of Manuscripts Accepted (2023)

:stressbiol@nwafu.edu.cn stressbiol@gmail.com
:+86-29-87082877 :@stressbiology
https://link.springer.com/journal/44154
https://www.editorialmanager.com/sbio

Springer

华安生物
HUABIO

抗体 | 蛋白 | ELISA Kit | 定制服务

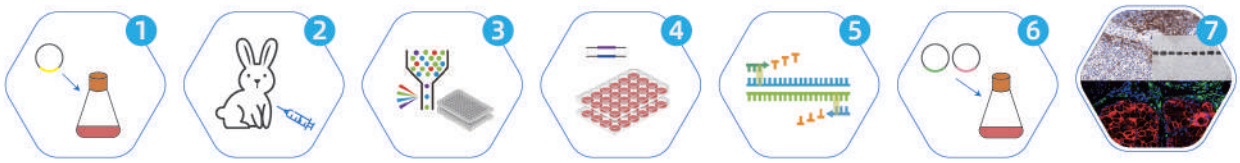
杭州华安生物技术有限公司成立于2007年，总部位于浙江杭州。公司致力于为全球生命科学领域的科学家、体外诊断以及生物医药领域提供高品质的生物试剂产品和解决方案。

公司采用基于结构生物学的抗原设计，单克隆B细胞筛选的重组抗体开发，以及多维度的质量验证体系等，一系列有自主专利保护的技术和流程，研发、生产具有高灵敏性，高特异性，无批次差异的核心抗体产品，解决了传统抗体工艺的长期痛点。由多名博士组成的科学家团队专注于抗体发现和抗体验证，不断提升抗体研发和应用的技术水平。

公司肩负“为推动生命科学发展，提供优质产品和服务”的使命，用产品来帮助科学家们突破难题，助力研究成果在*Science*、*Nature*、*Immunity*、*Cell*等顶级期刊发表。

HiMab™华安生物重组兔单抗平台

通过HiMab™重组兔单抗平台研发了近4000种重组兔单抗，覆盖细胞生物学、表观遗传学、信号转导等热门研究领域。



Immunogen preparation | Rabbit immunization | Single B cell sorting | Antibody preparation&screening | Antibody sequencing | Antibody production | Antibody validation

平台优势

- 高亲和力和特异性
- 重组技术带来的批次间一致性
- 天然多样性，可筛选多表位
- 可进行重组改造（人源化）
- 无动物源性

定制服务

单克隆抗体服务

- 常规鼠单抗制备
- 功能性抗体制备
- 配对抗体制备
- 重组兔单抗制备

多克隆抗体服务

- 标准多克隆抗体制备
- 修饰性抗体制备
- 抗独特型抗体制备
- 小分子抗原抗体制备

蛋白表达和纯化服务

- 全基因合成
- 质粒构建
- 蛋白表达和纯化

其他单项服务

- 多肽合成
- 蛋白的交联/标记
- 腹水制备和纯化
- 重组抗体表达

杭州华安生物技术有限公司

Hangzhou HuaAn Biotechnology Co.,Ltd

地址：杭州市钱塘新区白杨街道6号大街452号高科技企业孵化园区2号楼16层D区
邮编：310012　　邮箱：sales@huabio.cn
电话：0571-88062880　传真：0571-88060400

聚焦抗体，专业服务！ **www.huabio.cn**
国内免费销售热线：*4008-123-175*

平安陳®

PING AN CHEN

Established
Pingantan Pharmacy in 1950

平安陈 百年藏

Ping An Chen is a collector of century-old dried tangerine peel

Ping An Chen est un collectionneur de peau de mandarine séchée centenaire

Ping An Chen ist ein Sammler von hundertjähriger getrockneter Mandarinenhaut

平安陳は百年物の陳皮コレクター

GemPharmatech™

GemPharmatech Developed World's Largest and High-quality Mouse Model Resources

Knockout All Project (KOAP)
Disease Mouse Models
Immunodeficient Mouse Models
Humanized Immune Checkpoint Mouse Models
Reliable, High-quality and Cost-effective Preclinical Services

Headquarters
12 Xue fu Road, Jiangbei New Area District Nanjing,
210061, P.R. China

globalservice@gempharmatech.com
www.gempharmatech.com
+86-25-58641508

MCE MedChemExpress

www.MedChemExpress.cn

Inhibitors • Screening Libraries • Proteins

80,000+ 高纯度小分子

- 抑制剂 & 拮抗剂
- 天然产物
- 同位素标记物
- 荧光染料/探针
- GMP 小分子
- 标准品
- PROTACs & PROTAC 相关
- 点击化学
- 生化试剂
- 定制服务

60,000+ 高活性生物大分子

- 重组蛋白
- 多肽
- 一抗 & 二抗
- 抗体抑制剂
- 寡核苷酸
- 酶
- ADCs & ADC 相关
- 定制服务

MCE 一站式药物筛选平台

- 化合物库
  - 生物活性化合物库
  - 类药多样性库
  - 片段化合物库等
  - 定制服务
- 筛选服务
  - 虚拟筛选
  - DNA 编码化合物库 (DEL) 筛选
  - 表面等离子共振 (SPR) 检测服务等
- 先导化合物优化

高效生物试剂盒

- 抑制剂 Cocktails
- RT/qPCR & PCR 预混液
- 免疫磁珠 & 琼脂糖
- 蛋白生物学
- 2D/3D 细胞培养
- 细胞分析

全球数十万科学家的共同选择

全球合作伙伴

Roche · 北京大学 PEKING UNIVERSITY · NUS · Dana-Farber Cancer Institute · MilliporeSigma · 清华大学 Tsinghua University · Takeda · Karolinska Institutet · Lilly · Calibr · AstraZeneca · gsk · NOVARTIS · Yale University

积分享不停 关注公众号

MCE 中国

400-820-3792 | 021-58955995

sales@MedChemExpress.cn

RAYME
瑞 明 生 物 科 技

实时单细胞多功能分析仪

功 能

实时单细胞多功能分析仪可以实时、连续、定量检测单个活细胞的代谢类小分子含量及酶活性，该产品补充了单细胞研究对新检测技术的需要，帮助用户更好的理解细胞组成、生理行为与功能的多样性。

特 点

1、高时空分辨率:单细胞及亚细胞水平(细胞质、细胞核)实时、原位、定量检测；
2、多种检测指标:开放试剂盒，单个活细胞多种小分子含量(如乳酸，ATP，ROS等)及酶活性(葡萄糖甘酶等)检测；
3、单细胞提取注射:提取细胞内容物或细的器(如溶酶体、线粒体)进行质谱分析、测序、酶活性分析;或注射药物、底物到细胞内进行药效评估等；
4、活体检测:可在活体水平上检测特定穴位处生化指标的变化，研究药物起效机理。

产品应用

细胞代谢　　肿瘤机制
新药研究　　生物纳米材料
神经科学　　中医针灸

江苏瑞明生物科技有限公司
JIANGSU RAYME BIOTECHNOLOGY CO.,LTD

地址：江苏宜兴市经济开发区杏里路10号光电产业园1栋7楼
电话：0510-80328166
邮箱：sales@raymetech.com
网站：www.raymetech.com

扫码关注 了解更多

喀斯玛(北京)科技有限公司是中国科学院控股有限公司旗下国有企业。于2013年创建了服务科研领域的垂直型B2B+O2O第三方电子商务平台，集交易、管理、资讯为一体，以网络超市和信息化管理模式，实现了科研物资采购及管理的规范、安全、便捷。平台业务范围涵盖生物试剂及耗材、化学试剂、科研仪器及维修、技术服务、办公用品、元器件、农资农具、实验气体等。入网供应商9000余家，在线商品1.7亿条，全国超2600家科研、教育、医疗及产业机构应用本平台，服务了107个院士团队，保障了超254亿元国家科研经费的规范使用。十年来，喀斯玛获得了多项资质与荣誉，已成为国内重要的科技创新服务实体。

扫码关注
喀斯玛订阅号

BRS

BQC REDOX SYSTEM

总抗氧化能力检测仪

一种新型的电化学法、简单、快速、精确、多参数、便携式的设备
用于评估 **总抗氧化状态(TAC)** 和 **H_2O_2清除能力**

特点：

直接、快速

无有机溶剂

无自由基引发剂

无需样品预处理

轻松得到实验结果

无需其他昂贵的仪器

无需分光光度计和荧光计

无需专业技术人员

总抗氧化能力

BRS检测TAC仅需1min
且无需复杂的样品预处理。

一键测试多参数

饮料类：抗坏血酸、多酚、TAC
红酒类：抗坏血酸、多酚
油类：维生素E、TAC、氧化作用

H_2O_2清除能力

BRS只需两步即可检测H_2O_2清除能力，无需繁琐的光学法检测。

BRS适用样品

血液
血清
血浆
细胞和组织
尿液
唾液
饮料
提取物
粉末
其他

HI£
I'm fluidlad R-300
便携式细胞计数仪&光谱仪

anvajo

全自动细胞计数

光谱分析

动力学测量

细胞计数

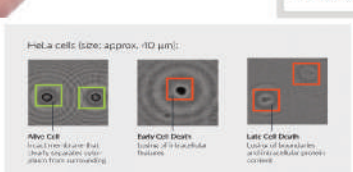
全息显微技术
免染色活率分析
大视场细胞计数
样本量仅需4-20ul

免染色
细胞存活率分析

标准曲线

光谱分析

375-700nm波长
光谱扫描
OD600测定
动力学分析
小巧、便携



Bioquochem(BQC)总抗氧化能力检测仪

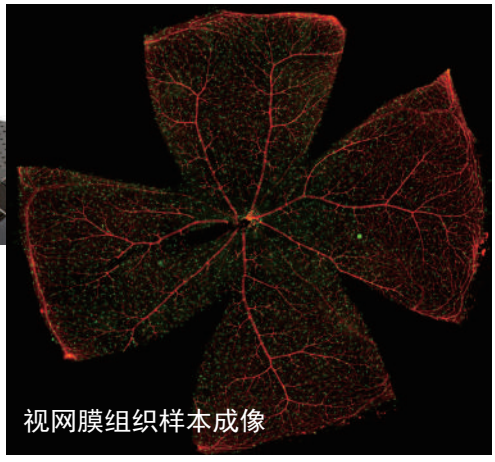
德国anvajo 免染色细胞计数仪&光谱仪

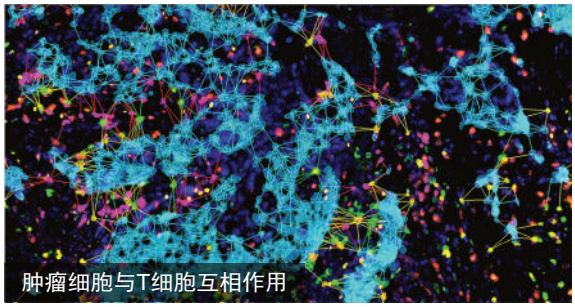
中国区总代理及技术服务中心：
上海怡赛科学仪器有限公司
Shanghai E-sci Scientific Instrument Co., LTD

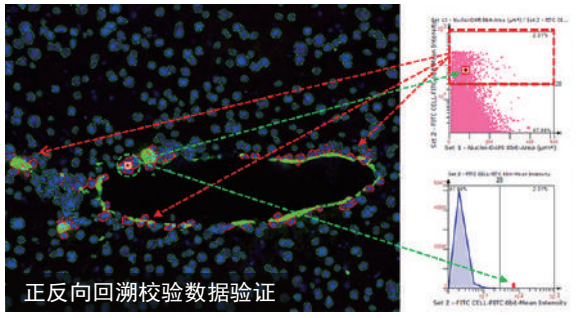
电话：021-67898557
邮箱：xpf@e-sci.com.cn
网址：www.e-sci.com.cn

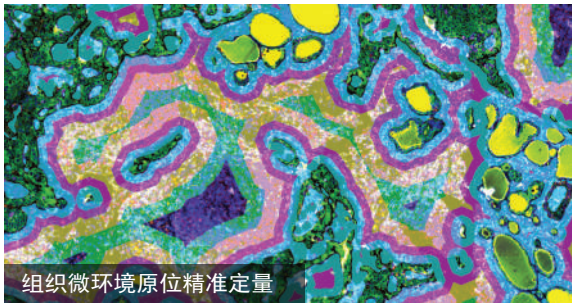
<<<TissueFAXS Q+ XY全景+Z轴全景深成像定量分析系统

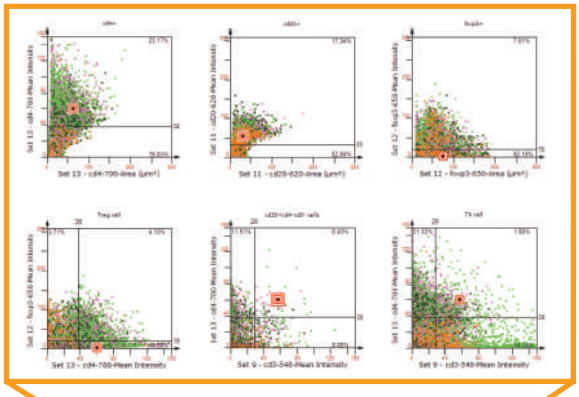
TissueFAXS Q+ 多维跨尺度高清超快速全景组织成像定量分析系统，可实现组织或器官层面跨模态、大尺度高清晰度共聚焦快速全景成像，以病人样本、实验动物样本、动物模型样本等为研究对象，深度挖掘组织（实体瘤、脏器、靶器官等）内或器官横切面蕴含的组织微环境分析大数据，构建临床研究辅助诊断体系，辅助临床科学研究实现精准诊疗，可以对医学实验动物（斑马鱼、大小鼠、实验猴、猪等）组织原位体内微环境进行深度解析和分析性研究，对体内蛋白或核酸原位精细定位量化分析、进行组织类流式分析，以及空间位置关系等微环境生物学研究。

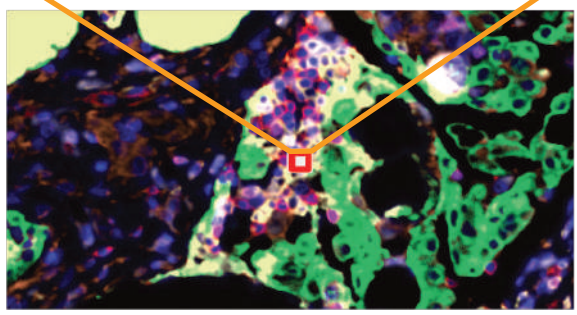

视网膜组织样本成像


肿瘤细胞与T细胞互相作用


正反向回溯校验数据验证


组织微环境原位精准定量





<<<神经学方向研究

神经干细胞、星形胶质细胞、脑功能、神经退行性疾病，如帕金森、阿尔兹海默等细胞体和神经突起的大小、长度、分支数量进行识别定量，并根据不同功能与不同区域，区分单极、多级神经元。利用形态学识别的方法，在多种不同样本类型中，识别出神经元胞体和突起。按照神经元外型的差异，在免疫组化样本中，对细胞体和神经突的大小、长度、分支数量进行识别定量，并根据不同功能与不同区域，区分单极、多级神经元。

北京华威中仪
展位号B5

Huawei
Better work . Better life

提供组织-细胞-线粒体多参数一站式实时检测方案

Provide a one stop real-time detection solution for tissue-cell-mitochondrial multi-parameters

OROBOROS INCYTON

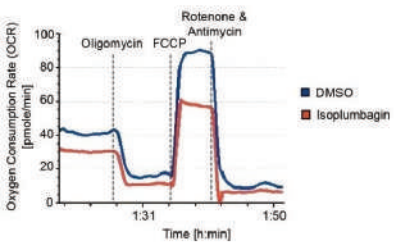
奥地利 OROBOROS O2k 高精度线粒体氧化磷酸化功能表征系统

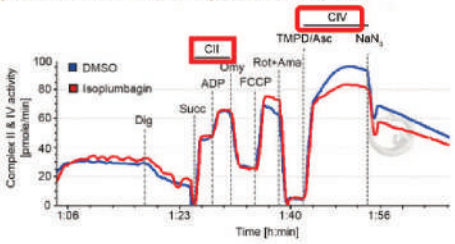
HIGHPRECISION MITOCHONDRIAL OXIDATIVE PHOSPHORYLATION FUNCTIONAL CHARACTERIZATION SYSTEM

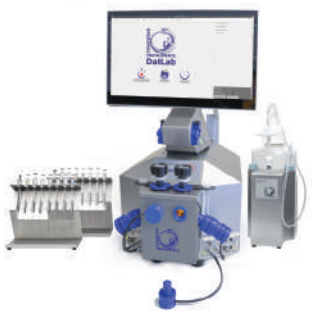
多参数检测（Multi-parameter detection）：pO_2、pH、ATP、MMP、ROS、Ca^{2+}、CoQ、NADH、NO、H_2S、TPP^+
多样品适用（Suitable for multiple samples）：组织（Tissues）、细胞（cells）、线粒体（mitochondria）、血液（blood）、细菌（bacteria）
精准检测方式（Accurate detection method）：极谱氧电极传感器检测，精准度更高
Polarographic oxygen electrode sensor detection with higher accuracy
开放试剂（Open reagents）：可自行设计实验，同时提供 67 种 Protocol 可供选择
Design your own experiments and choose from 67 protocols
应用方向（Application direction）：Cancer、Cardiovascular、Neurological、Aging、Drugs、Exercise Physiology、 Mitochondrial Medicine etc

深度表征线粒体氧化磷酸化各个复合体的功能活性检测

In-depth characterization of mitochondrial oxidative phosphorylation of the functional activity of various complexes







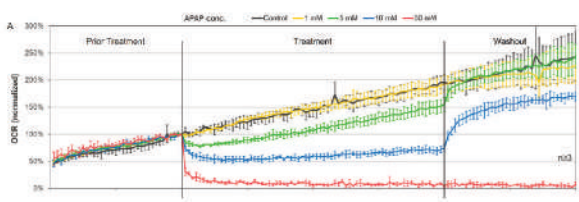
德国 INCYTON 智能多维度细胞长周期全息分析平台

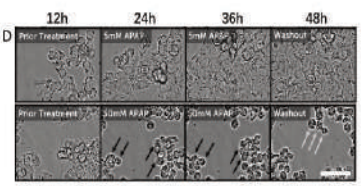
INTELLIGENT MULTI DIMENSIONAL CELL LONG CYCLE HOLOGRAPHIC ANALYSIS PLATFORM

技术特点（Technical features）：无标记检测（Mar freedetection）、多维度分析（multi dimensional analysis）、
长时间监测（long term monitoring）、全自动操作（fully automatic operation）
检测参数（Detection parameters）：pH、pO_2、Impedance、image
应用领域（Fields of application）：细胞毒理（Cytotoxicology）、安全性评价（safety evaluation）、细胞治疗研究（cell therapy research）、
肿瘤医学（Oncology），代谢组学（metabolomics）、药物筛选（Drug screening）
实时显微成像技术同步精确整合，实现几天、几周到数月的长时间细胞活性无标记监测与分析
Real-time microscopy technology is precisely integrated to enable label-free monitoring and analysis of cell viability over long periods of time, from days to months

对乙酰氨基酚(APAP)对人肝细胞(HepG2)毒性作用

Acetaminophen (APAP) toxic effects on human hepatocytes (HepG2)





OROBOROS INSTRUMENTS

INCYTON

北京华威中仪科技有限公司
地址：北京市丰台区汽车博物馆东路盈坤世纪G座504
电话：010-83659327
邮箱：huawei@hwsci.com