Michigan Medicine -
Peking University Health Science Center
Joint Institute for Translational and Clinical Research

北京大学医学部-密西根大学医学院
临床与转化医学联合研究所

Eighth Annual Symposium

第八届学术研讨会

October 15-17, 2018
Ann Arbor, Michigan

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Dear Colleagues:

On behalf of the University of Michigan Medical School and Peking University Health Science Center, we are excited to welcome you to the Eighth Annual Symposium of the Michigan Medicine-Peking University Health Science Center Joint Institute (JI) for Translational and Clinical Research.

This marks the fourth time that UMMS has hosted our PKUHSC colleagues. As always, we have much to share and celebrate over the course of our busy three-day agenda. We'll highlight much of the important work that is ongoing within the JI and we'll spend a lot of time talking about growing areas of interest and collaborations between our institutions, including precision health and mental health. We look forward to engaging conversations about the ways we are exploring – and will continue to explore – our JI partnership.

Within this program book you will find introductions to the Joint Institute, Michigan Medicine, the University of Michigan Medical School, and the Peking University Health Science Center. Overviews of each of the JI research programs and cores, as well as information about the new JI projects, are included to provide a foundation for the symposium presentations. Biographical information for our speakers and guests from China are also included, as are the abstracts for the Keynote addresses. At the back of the program you will find contact information for lodging, transportation, emergency services, and Global REACH staff.

We are excited to have this opportunity to share with you the outstanding progress being made on our very unique platform for clinical and translational research. As with past meetings, we hope that new friendships will lead to future collaborations and research ideas. Enjoy the symposium activities and your stay in Ann Arbor!

Sincerely,

Joseph C. Kolars, MD
Co-Director
Michigan Medicine-PKUHSC Joint Institute
Senior Associate Dean for Education
and Global Initiatives
Josiah Macy, Jr., Professor of Health
Professions Education
University of Michigan Medical School

Qimin Zhan, PhD
Co-Director
Michigan Medicine-PKUHSC Joint Institute
Executive Vice President, Peking University
President, Peking University Health Science
Center

各位参会嘉宾：

我们谨代表密西根大学医学院和北京大学医学部，衷心地欢迎大家参加第八届北京大学医学部–密西根大学医学院临床与转化医学联合研究所年度学术研讨会。

今年是密西根大学医学院第四次作为东道主举办研讨会。三天的会议将围绕联合研究所目前的项目进行汇报讨论，与此同时，我们还探讨双方崭新的合作机会，包括精准医学和心理健康等领域。我们期望通过此次大会，推进现有合作，并探索新的合作可能性。

本手册为大家提供了我们联合研究所、密西根大学医学院以及北京大学医学部的简要介绍。同时，我们也收录了联合研究所各个合作项目与核心支撑平台的概况以作为您聆听大会汇报的参考。本手册还收录了大会特邀嘉宾和来自中国的贵宾名单和简历，以及大会发言摘要。手册最后附上了大会住宿、交通、应急服务、以及工作人员的联系方式。

通过本次盛会，我们真诚地希望能与大家分享我们在联合研究所的绝佳合作平台上所取得的显著成就。我们也希望此次盛会，一如既往地促进双方友谊，推动合作意愿及加深合作关系。我们衷心地希望您喜欢本次研讨会各项活动，祝美国之旅一切顺利。

Joseph C. Kolars, MD
约瑟夫•考拉斯教授
联合研究所执行委员会共同主席
密西根大学医学院教育与全球发展资深副院长
密西根大学医学院医疗职业与教育学荣誉教授

Qimin Zhan, PhD
詹启敏教授
联合研究所执行委员会共同主席
北京大学常务副校长
北京大学医学部主任

2018 Symposium Overview
大会一览表

Monday, October 15				Tuesday, October 16			Wednesday, October 17	
			7:15	Shuttle to BSRB				
			7:50	Group Photo				
8:00	Shuttle to Medical Science Building I		8:00	Welcome & Opening Ceremony			8:00	Shuttle to BSRB
8:30	Meet U-M team members at Medical Science Building I		8:20	Plenary Speech I			8:30	Plenary Speech III
9:00	Individual Project/Lab/ Investigator Meetings*		9:00	Plenary Speech II			9:10	Plenary Speech IV
10:00	Cancer Research Session*		9:40	Break			9:50	Break
			10:00	Panel: Precision Health & Cancer			10:00	Panel: Precision Health & Mental Health
noon	Lunch	Medical Education Session*	noon	Lunch	JI Executive Board Mtg*		noon	Lunch
2:00	Leadership & Development Council Tour*		1:30	JI Program Concurrent Sessions			1:30	Select JI Project Presentations
			3:30	Break			3:45	Wrap-Up & Closing Remarks
			3:45	Poster Session				
			5:00	Shuttle to U-M Golf Course			4:00	Shuttle to hotel
			5:30	Banquet Reception*				
6:00	Team Dinners*		6:00	Banquet*				
			8:30	Shuttle to hotel				
** Denotes by invitation only*								

Location Key:

- Varies by Project/Program
- A. Alfred Taubmanb Biomedical Science Research Building (BSRB)
- U-M Golf Course Clubhouse
- Palmer Commons
- A. Alfred Taubman Health Sciences Library

2018 Symposium Overview
大会一览表

Monday, October 15				Tuesday, October 16			Wednesday, October 17	
			7:15	乘车前往BSRB				
			7:50	嘉宾合影				
8:00	乘车前往Med Sci I		8:00	开幕式致辞			8:00	乘车前往BSRB
8:30	与UM团队成员在Med Sci I 会面		8:20	大会主旨发言: Dr. Eric Fearon			8:30	大会主旨发言:Dr. Steve Kunkel
9:00	合作项目分组活动		9:00	大会主旨发言：张小田教授			9:10	大会主旨发言: 张宁教授
10:00	肿瘤研究合作研讨会*		9:40	茶歇			9:50	茶歇
			10:00	专题论坛：精准医疗与癌症			10:00	专题论坛：精准医疗与心理健康
noon	午餐	医学教育合作研讨会	noon	午餐	联合研究所董事会议*		noon	午餐
2:00	发展咨询理事会论坛		1:30	联合研究所项目分组论坛			1:30	精选联合研究所项目汇报
			3:30	茶歇			3:45	总结报告及闭幕式
			3:45	海报展示				
			5:00	乘车前往U-M高尔夫球场			4:00	乘车返回酒店
			5:30	餐前招待会				
6:00	团队晚餐		6:00	晚宴				
			8:30	乘车返回酒店				
*邀请制								

会议地点:

- Varies by Project/Program
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2018 Symposium Detailed Schedule
大会详细日程安排

Tuesday, October 16, 2018 MORNING SESSION		
All events open to the public unless otherwise noted		
TIME	**EVENT**	**LOCATION**
7:15 a.m.	Shuttle from hotel to Biomedical Science Research Building (BSRB)	
7:50 - 8:00 a.m.	**Group Photo**	BSRB Gilbert S. Omenn Atrium
8:00 - 8:20 a.m.	**Welcome & Opening Ceremony** Joseph C. Kolars, MD *(pg. 91)* Sr. Associate Dean for Education & Global Initiatives, UMMS Marschall S. Runge, MD, PhD *(pg. 93)* Exec. Vice President for Medical Affairs, Michigan Medicine Mark Schlissel, MD, PhD *(pg. 94)* President, University of Michigan Qimin Zhan, MD *(pg. 80)* Executive Vice President, PKU; President, PKUHSC	BSRB Kahn Auditorium
8:20 - 9:00 a.m.	**Plenary I: Dogma, Paradigm Shifts, and Recurring and Emerging Themes in the Cancer Field** *(pg. 22)* Eric Fearon, MD, PhD Director, U-M Rogel Cancer Center Emanuel N. Maisel Professor of Oncology Professor of Human Genetics, Internal Medicine & Pathology	
9:00 - 9:40 a.m.	**Plenary II: Precision Drug Therapy for Gastric Cancer: Current Status and Future Directions** *(pg. 23)* Xiaotian Zhang, MD Professor of Gastrointestinal Oncology Deputy Director, Office of International Affairs Peking University Cancer Hospital	
9:40 - 10:00 a.m.	**Break**	
10:00 a.m. - noon	**Panel I: The Promise & Perils of Precision Health for Cancer** *Moderators* Qimin Zhan, MD *(pg. 80)* Executive Vice President, PKU; President, PKUHSC Eric Fearon, MD, PhD *(pg. 90)* Director, U-M Rogel Cancer Center *Panelists* Arul Chinnaiyan, MD, PhD *(pg. 89)* Professor of Pathology, UMMS Kaifeng Pan, MD, PhD *(pg. 65)* Director, Cancer Epidemiology Dept., PKUHSC J. Scott Roberts, PhD *(pg. 93)* Professor of Health Behavior & Health Education, UM Jianmin Wu, PhD *(pg. 74)* Professor of Bioinformatics, PKUHSC Thomas Wang, MD, PhD *(pg. 95)* Professor of Internal Med., Biomedical Engineering, UMMS Lianhai Zhang, MD *(pg. 82)* Chief Surgeon, Gastrointestinal Surgery, PKUHSC Anne Schott, MD *(pg. 94)* Assoc. Director for Clinical Research, U-M Rogel Cancer Center Yan Kong, PhD *(pg. 58)* Assoc. Professor of Renal Cancer and Melanoma, PKUHSC	

2018 Symposium Detailed Schedule
大会详细日程安排

Tuesday, October 16, 2018	AFTERNOON SESSION	
All events open to the public unless otherwise noted		
TIME	**EVENT**	**LOCATION**
noon-12:15 p.m.	Walk to Palmer Commons	
12:15-1:15 p.m.	Lunch	Palmer Commons Great Lakes Rooms
noon-1:30 p.m.	Executive Board Meeting*	THSL 6000
1:30-3:30 p.m.	JI Program Concurrent Sessions	
	Cardiovascular Diseases	BSRB Kahn Auditorium
	Lung Disease	BSRB 3515
	Liver/GI Disease	BSRB 5515
	Dentistry	THSL 5000
	Psychiatry	BSRB 4008
	Satellite Meetings on Other Projects	Rooms vary by project
3:30-3:45 p.m.	Walk to BSRB	
3:45-5:00 p.m.	Poster Session	BSRB Gilbert S. Omenn Atrium
4:00-5:00 p.m.	Leadership & Development Council Meeting*	U-M Golf Course Clubhouse
5:00-5:30 p.m.	Shuttle to U-M Golf Course Clubhouse	
5:30-6:00 p.m.	JI Banquet Reception*	U-M Golf Course Clubhouse
6:00-8:30 p.m.	JI Banquet*	U-M Golf Course Clubhouse
8:30 p.m.	Shuttle to hotel	
*Denotes invitation-only event		

2018 Symposium Detailed Schedule
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Wednesday, October 17, 2018 MORNING SESSION		
All events open to the public unless otherwise noted		
TIME	**EVENT**	**LOCATION**
8:00 a.m.	Shuttle from hotel to Biomedical Science Research Building (BSRB)	
8:30-9:10 a.m.	**Plenary III: Strategic Research Planning and Priorities: Responding to Change and Securing the Future** *(pg. 24)* Steven Kunkel, PhD Senior Associate Dean for Research, Medical School Endowed Professor of Pathology, UMMS	BSRB Kahn Auditorium
9:10-9:50 a.m.	**Plenary IV: Strategic Research Planning at PKUHSC** *(pg. 25)* Ning Zhang, PhD Vice President, PKUHSC	
9:50-10:00 a.m.	Break	
10:00 - noon	**Panel II: The Promise & Perils of Precision Health for Mental Health** *Moderators* Lin Lu, MD, PhD *(pg. 63)* Director, Institute of Mental Health, PKUHSC 6th Hospital Frederic Blow, PhD *(pg. 88)* Professor of Psychiatry, UMMS *Panelists* Chad Brummett, MD *(pg. 89)* Associate Professor of Anesthesiology, UMMS Lin Lu, PhD *(pg. 63)* Director, Institute of Mental Health, PKUHSC 6th Hospital Amy Bohnert, PhD, MHS *(pg. 89)* Associate Professor of Psychiatry, UMMS Srijan Sen, MD, PhD *(pg. 93)* Professor of Depression and Neurosciences, UMMS Ping Wu, MD, PhD *(pg. 74)* National Institute on Drug Dependence, PKU	

2018 Symposium Detailed Schedule
大会详细日程安排

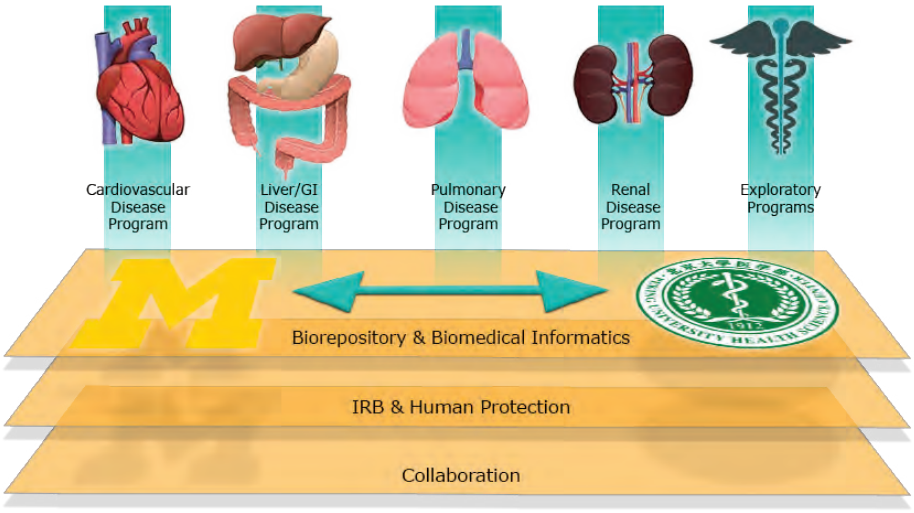
Wednesday, October 17, 2018 AFTERNOON SESSION		
All events open to the public unless otherwise noted		
TIME	**EVENT**	**LOCATION**
noon-12:15 p.m.	Walk to Palmer Commons	
12:15-1:15 p.m.	Lunch	Palmer Commons Great Lakes Rooms
1:15-1:30 p.m.	Walk to BSRB	
1:30-3:45 p.m.	**JI Program Select Presentations**	BSRB Kahn Auditorium
1:30-1:50 p.m.	Particulate Matter Air Pollution and High Density Lipoprotein Dysfunction Jianping Li, MD, PhD *(pg. 59)* Professor of Cardiology, Peking University First Hospital	
1:50-2:10 p.m.	Effects of Diet and Genetic Factors on Gut Gysbiosis in IBS Liping Duan, MD *(pg. 53)* Professor of Gastroenterology, PKU Third Hospital	
2:10-2:30 p.m.	Compartmental Analysis of Metabolite Profiles Associated with Disease Phenotypes in Chinese and US Smokers with and without COPD Kathleen Stringer, PharmD *(pg. 95)* Albert B. Prescott Professor of Pharmacy, U-M MeiLan Han, MD, MS *(pg. 91)* Professor of Pulmonary Medicine, Critical Care, UMMS	
2:30-2:45 p.m.	Break	
2:45-3:05 p.m.	Identify Smooth Muscle Cell Specific Protein as Biomarkers for Early Diagnosis of Acute Aortic Dissection Zhe Zhang, MD *(pg. 84)* Vice Director of Cardiac Surgery, PKU Third Hospital	
3:05-3:25 p.m.	Targeting Peptidylarginine Deiminase (PAD) for Diagnosis and Treatment of Severe Inflammation Hasan Alam, MD *(pg. 88)* Section Head of General Surgery, UMMS	
3:25-3:45 p.m.	Urine Protein Glycosylation and Progression of Chronic Kidney Disease Subramanian Pennathur, MD *(pg. 92)* Division Chief of Nephrology, UMMS	
3:45-4:00 p.m.	Wrap-Up & Closing Remarks	
4:00 p.m.	Shuttle to hotel	
*Denotes invitation-only event		

Introduction to the Joint Institute for Translational and Clinical Research

Overview

In 2010, the University of Michigan Medical School (UMMS) and Peking University Health Science Center (PKUHSC) signed an unprecedented agreement to establish a Joint Institute (JI) for Translational & Clinical Research. Each institution contributed $7 million for the 2010 launch and both renewed their financial commitment with repeat $7 million investments in 2015, securing the JI and the international collaboration for years to come.

Much of the research focuses on four key areas of interest to both institutions: cardiovascular, liver, pulmonary, and renal diseases. At the same time, Infrastructure "Cores" – Biorepository and Biomedical Informatics; Collaboration; IRB and Human Protection – help the partners overcome specific challenges or concerns associated with global collaboration. The annual JI Symposium, held on alternating years in Beijing and Ann Arbor, brings all of the researchers from both institutions together to share progress, advance projects, and forge new partnerships.



Michigan Medicine-PKUHSC JI Programs & Cores Structure

Select updates from the previous year

- PKU First Hospital Pediatrician Xuhui Zhong spent all of 2017 at Michigan Medicine learning clinical research techniques in the lab of Professor of Pediatrics Debbie Gipson.
- Joint institute Leadership and Development Council held its first official meeting on Sept. 25, 2017 during the Seventh Annual JI Symposium in Beijing. Comprised of prominent Chinese philanthropists and healthcare business leaders, the council will advise, inspire and support the future of JI. On May 19, 2018, the council met the second time to discuss the strategies and road map of the JI.
- Michigan Medicine Pediatrics Resident Mark Kluk visited PKU First Hospital in March 2017 to complete a clinical rotation as well as launch a research project exploring how Chinese medical students perceive the value of international educational experiences.
- A group of ten hospital administrators from PKU Third Hospital became the first to complete a three-week pilot Executive Training Program hosted by Michigan Medicine and Global REACH in June 2017.
- PKU Third Hospital's Qingbian Ma, Chief Physician and Vice Chair of Emergency Medicine, spent July and August 2017 in Ann Arbor doing an observership with Michigan Medicine Emergency Medicine Chair Robert Neumar and other colleagues.
- PKU Second Hospital Trauma and Orthopedics Attending Physician Jing Zhou began a year-long research rotation at Michigan Medicine in November 2017, working in the lab of Professors of Surgery Hasan Badre Alam and Yongqing Li.
- PKUHSC Director of the Office of International Cooperation Quidan Sun led a delegation of JI leaders to Ann Arbor in December 2017 for a multi-day meeting focused on the partnership's three research cores.
- A 2018 Call for Proposals received a record 33 letter of intent responses from faculty interested in launching new JI research projects. 10 teams were selected to receive funding, including projects in Cardiovascular, GI, Pulmonary, Renal, Pediatric, and Dermatology.
- UMMS Director of China Programs Amy Huang visited PKUHSC Shenzhen Hospital in April 2018 to discuss potential collaborations as part of an effort to expand the reach of the JI beyond Beijing to include other PKUHSC-affiliated hospitals in China.
- Dr. Joe Kolars attended the opening ceremony for National Medical Education Development Center at PKUHSC on May 16, 2018. Dr. Kolars is the only foreign member of the Center's Advisory Committee. He also delivered the keynote at the New Era Medical Education reform and Development Forum.
- PKUHSC inaugurated the National Key Center for International Cooperation in May 2018.
- Michigan Medicine and PKUHSC finalized plans to launch a dual master's degree program in bioinformatics during a meeting which brought PKUHSC Dean of Basic Medical Sciences Yuxin Yin and others to Ann Arbor in May 2018.

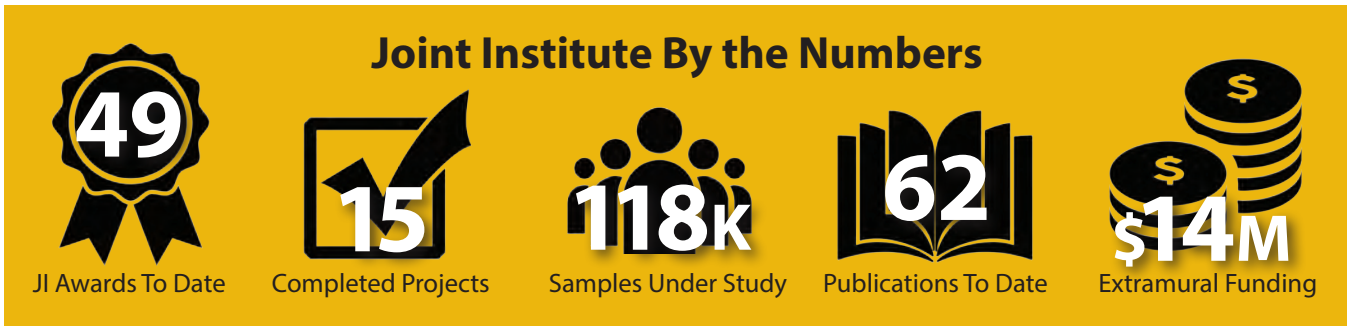
简介

2010年10月，北京大学医学部和美国密西根大学医学院正式合作并成立了北京大学医学部-密西根大学医学院临床与转化医学联合研究所。该联合研究所是双方科研合作的平台，由双方共同投入1400万美元的资金，启动联合科研项目，利用双方现有的优势资源推进世界健康。2015年，双方再次共同投入1400万美元，开始第二个五年合作。

联合研究所初期的合作重点为心血管疾病、肝病、呼吸疾病和肾病领域，目前已组建了双方合作的专家团队。通过这个平台，基础科学的研究成果能更快更有效地转化到临床应用，推动中美乃至世界健康。此外，为了保证双方合作项目的顺利进行，联合研究所还建立了三个核心支撑平台，包括：生物样本库和生物信息平台，伦理委员会及受试者保护平台，以及国际合作科学研究管理平台。为了进一步推进科研合作，加强双方交流，联合研究所提供了一系列的交流合作平台，包括举行年度研讨会和讲座，支持教师、医学生、和住院医生的互动交流，提供学术信息，以及进行国际合作科学研究等等。

过去一年要闻回顾

- 2017年，北京大学第一医院儿科医生钟旭辉在密西根大学医学院儿科教授Debbie Gipson的实验室学习临床研究技术。
- 2017年9月25日，在北京召开的第七届联合研究所年度学术研讨会上， 联合研究所发展咨询理事会召开了第一次正式会议。参会者包括杰出的中国慈善家与医疗商业领军人物。发展咨询理事会对联合研究所未来的发展给予建议和支持。2018年5月19日，发展咨询理事会召开了第二次会议， 讨论联合研究所的发展战略与目标。
- 密西根大学医疗中心儿科住院医生Mark KluK于2017年3月访问了北京大学第一医院， 完成了临床实习并启动了研究中国医学生对海外交流经历评估的研究项目。
- 2017年6月，10位来自北京大学第三医院的行政人员成为了第一批完成为期3周的行政管理培训试点项目的学员。 这个试点项目由密西根大学医学院和Global REACH办公室协同创立。
- 2017年7月和8月，北京大学第三医院的主任医师兼急诊科副主任马青变在密西根大学医学院急诊科主任Robert Neumar与其他教授的指导下，进行了参观学习。
- 2017年11月，北京大学第二医院创伤与整形外科主治医师周靖在密西根大学医学院外科教授Hasan Alam 和Yongqing Li的指导下，开始了为期一年的科研轮转。
- 2017年12月，联合研究所三个核心支撑平台交流研讨会在安娜堡召开，与会人员就联合研究所的管理规范化及发展进行了讨论。
- “2018科研课题征集”收到了33项新的科研项目意向书。10个科研项目获得了联合研究所的资金资助,选中的项目包括心血管，胃肠道,肾病,儿科，以及皮肤病的研究。
- 密西根大学医学院中国项目主任Amy Huang在2018年4月访问了北京大学深圳医院，并讨论了潜在的合作可能性，将联合研究所在北京的影响力延伸到其他北京大学附属医院。
- 2018年5月16日，Joe Kolars院长参加了中国医学教育发展中心在北京大学医学部举办的开幕式。Joe Kolars院长是发展中心的咨询委员会里唯一的外籍成员，并且在新纪元医学教育改革与发展论坛上发表了主旨演讲。
- 2018年5月，中国科学技术部正式认定北京大学医学部-密西根大学医学院联合研究所为国家国际联合研究中心。
- 2018年5月，北京大学医学部基础医学院院长尹玉新与其同事前来安娜堡参加会议。会议上，密西根大学医学院与北京大学医学部为发起生物信息学双硕士学位项目一事确定了最终方案。



About Michigan Medicine

Twenty years after establishing its Medical School, the University of Michigan opened the first university-owned hospital in the United States in 1869. Today, Michigan Medicine is a nationally recognized leader in the care of patients, the advancement of innovation and research that improves human health, and in the education of the next generation of physicians, nurses, and scientists.

Michigan Medicine comprises three hospitals, more than 150 clinics across 40 locations, and an extensive home care operations network. In 2017, Michigan Medicine handled more than 54,000 surgical cases, and 100,000-plus emergency room/urgent care visits, in addition to 2.3 million outpatient visits. A dedicated team of nearly 30,000 outstanding faculty, staff, students, trainees, and volunteers treat patients from across the state of Michigan, the United States, and around the world.

Michigan Medicine is an academic health system with a stellar track record of sponsored funding, receiving about $601 million research dollars in 2017 and consistently ranking among the highest funded health research organizations in the United States. The hospital currently ranks No. 5 on U.S. News & World Report's national ranking of the country's top hospitals and has made the publication's list for 26 consecutive years.

About the University of Michigan Medical School

The Medical School was the University of Michigan's first professional school. Our faculty, students, and staff are proud to be part of the world-renowned University of Michigan, which includes top-ranked schools in Law, Business, Public Health, Nursing, Medicine, Dentistry, Social Work, and Pharmacy, as well as a premier health system. This unique opportunity for collaboration across so many disciplines sets the stage for innovation and gives us a strategic advantage when it comes to education, research, and patient care.

The University of Michigan Medical School (UMMS) accepts less than 3% of the 6,000-plus students who apply each year. The school graduates approximately 170 physicians annually, with a growing body of alumni that numbers more than 20,000. US News and World Report currently ranks UMMS as a top ten school in seven different areas: primary care, anesthesiology, biomedical engineering, internal medicine, women's health, radiology, and surgery. The school offers medical and scientific graduate degree programs, nearly 100 training programs for new doctors, hands-on learning for nursing and health professions students from UM and other institutions, and continuing-education courses for practicing physicians and nurses. UMMS also includes the University of Michigan Medical Group, which comprises about 1,800 faculty physicians from 20 clinical departments who care for patients at U-M hospitals and health centers.

From the beginning, we have known how to put patients first, when to push the boundaries of science and medicine, how to design successful curricula, and how to reward our faculty, students, and staff for their everyday excellence. Our Department of Learning Health Sciences, our 20 clinical and 9 basic science departments, and our Unit for Laboratory Animal Medicine are committed to a single mission: To educate students, physicians, and biomedical scholars and to provide a spectrum of comprehensive knowledge, research, patient care, and service of the highest quality to the people of the state of Michigan and beyond.

Visit www.medicine.umich.edu/medschool/ to learn more.

关于密西根大学医学院及医院

1869年，密西根大学医学院在成立20年后的1869年，建立了全美第一所大学附属医院。目前密西根大学医学院在病患护理，增强人类健康的创新研究，以及培养新一代医师、护士、科学家等方面是全美公认的领航者。

密西根大学医学中心拥有三所附属医院，还有分布在40个不同地点的150多个医疗诊所以及广泛分布的家庭医疗网络。2017年，我们有5.4万的手术病例，10万的急诊病例，以及高达230万的门诊人次。我们的团队由3万多名教职员工、学生、培训人员和志愿者组成，为来自于密西根州内外，全美及世界各地的病人提供服务。

密西根大学医学院2017年的科研经费赞助总数达6.01亿美元，排名跻身全美科研资助的大学前列。根据《美国新闻与世界报道》，密西根大学附属医院排名全美第五，连续26年位列全美最佳医院之列。

密西根大学医学院

密西根大学医学院是密西根大学设立的第一所专业学院。密西根大学拥有一流的医学院、法学院、商学院、公共卫生学院、护理学院、口腔医学院、社会工作学院以及药学院。这些名列前茅的学院，以及其极具声望的医学中心，使得密西根大学世界闻名。 作为当中的一份子，我们医学院的教职员工及学生校友们都深感自豪。这一多学科 / 跨学科的合作为我们的创新提供了崭新的平台，也为我们在教学、科研以及病患护理上提供了战略优势。

密西根大学医学院每年收到的入学申请高达6千多份，通常录取率少于3%。每年近170位医师毕业，加入日渐壮大的已有2万多人的校友会。根据《美国新闻与世界报道》，密西根大学医学院有七门学科跻身全美排名前十：家庭医学、麻醉科、生物医学工程、内科、放射科、妇科学和外科。我们设有医学及基础科学研究生学位，近100个专科医师培训项目，为来自密西根大学和其他学校的护理专业及医学专业的学生提供实践学习的机会，并为执业医师和护士提供继续教育的课程。密西根大学还拥有一个1,800名执业医师组成的联盟，他们在附属医院和医疗中心的20多个科室为病人提供服务。

一直以来，我们都铭记着把病患放在首位，推动科学和医学研究的前沿，设计实用而成功的教学大纲，以及鼓励表现卓越的教师、学生和工作人员，我们的20个临床医学，9个基础科学部门和1个动物实验基地致力于一个使命：培养优秀的学生、医生和生物医学者，并为密西根州内外的人民提供一个全面的学习、科研和高质量病患护理和服务的平台。

请浏览 www.medicine.umich.edu/medschool/ 了解更多。

Introduction to Peking University Health Science Center

As the most prestigious comprehensive medical institution in China, Peking University Health Science Center (PKUHSC) developed out of National Medical School of Peking, the first national school of western medicine established by the Chinese government through its own efforts. Since its inception in 1912, PKUHSC has cultivated a large number of high-level medical and health talents for the country, and has made outstanding contributions to improving the health of the Chinese people.

PKUHSC offers a full range of courses for its undergraduate programs, namely: basic medical sciences, clinical medicine, stomatology, preventive medicine, pharmaceutics, nursing, laboratory diagnosis, laboratory experiment and biomedical English and stomatology experiment technology. Postgraduate education at PKUHSC has a history of over 70 years. Currently, PKUHSC offers 67 academic doctoral programs, 17 professional doctoral programs, 71 academic Master's programs, and 23 professional Master's programs.

PKUHSC has five on-campus academic schools: School of Basic Medical Sciences, School of Pharmaceutical Sciences, School of Public Health, School of Nursing, and School of Foundational Education. PKUHSC now has an enrollment of 3,620 undergraduate students, 4,897 graduate students, and 424 international students. PKUHSC has 1 state key laboratory, 1 National Engineering Laboratory, 3 National Clinical Research Centers, 2 International Joint Research Centers, 41 ministry/city key laboratories, 2 Ministry Engineering Research Centers, 23 research institutes, and 60 research centers.

At present, PKUHSC has 10 affiliated hospitals: Peking University First Hospital, Peking University Second Hospital, Peking University Third Hospital, Peking University Stomatology Hospital, Peking University Sixth Hospital (Institute of Mental Health), Peking University Cancer Hospital, Peking University Shenzhen Hospital, Peking University Shougang Hospital, Peking University International Hospital and Peking University Binhai Hospital. PKUHSC also has 14 teaching hospitals in Beijing.

Since its merging with PKU, PKUHSC has been devoted to pursuing deeper integration between the two campuses. Now it endeavors to break the campus fence by implementing the concept of "Peking University Medicine", and thus contributes to the building of a greater PKU by encouraging resource consolidation and sharing, and fostering transdisciplinary collaboration, and co-creation between medicine and disciplines like engineering, natural sciences and social sciences.

For more information, please visit http://english.bjmu.edu.cn/ or contact the Office of International Cooperation, Peking University Health Science Center at oic@bjmu.edu.cn.

关于北京大学医学部

北京大学医学部（北医）是中国最知名的医学综合性院校，其前身是国立北京医学专门学校，是中国政府靠自己的力量开办的第一所专门传授西方医学的国立学校。自1912年创办以来，北医为国家培养了大批高水平的医药卫生人才，为提高人民健康水平做出了突出贡献。

北医现有10个本科专业：基础医学、临床医学、口腔医学、药学、预防医学、护理学、英语（生物医学英语方向）、医学实验学、医学检验和口腔实验技术。其研究生教育已有70余年历史。 现拥有67个学术博士学位授权点，17个专业博士学位授权点，71个学术硕士学位授权点和23个专业硕士学位授权点。

北京大学医学部设有5个学院：基础医学院、药学院、公共卫生学院、护理学院、公共教学部，共有本科生3620人，研究生4897人，留学生424人。北京大学医学部目前拥有1个国家重点实验室，1个国家工程实验室，3个国家临床研究中心，2个国际联合研究中心，41个部级/城市重点实验室， 2个教育部工程研究中心，以及23个校级研究所60个研究中心。

如今，北医已有10家附属医院，包括：北京大学第一医院、北京大学人民医院、北京大学第三医院、北京大学口腔医院、北京大学第六医院、北京肿瘤医院及北京大学深圳医院、北京大学首钢医院、北京大学国际医院和北京大学滨海医院等。此外，还有14家临床教学医院。

自从与北京大学强强合并后，北医正大鹏展翅，跨领域合作，与工程、自然科学及社会科学领域一起实现其最高目标：人类健康事业的发展

了解更多信息，请浏览北京大学医学部网站http://www.bjmu.edu.cn/，或邮件联系北京大学医学部国际合作处oic@bjmu.edu.cn。

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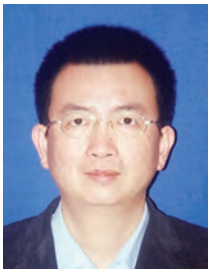

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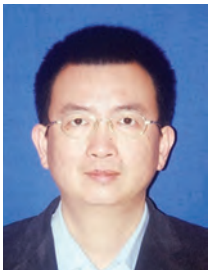

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COMPREHENSIVE CANCER CENTER
Helipad
stairs to staff parking steep incline
main entrance University Hospital & Taubman Center
U-M bus stop
Towsley Center
TAUBMAN CENTER
P2
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patient entrance
exit
Floor 2 Connector
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UNIVERSITY OF MICHIGAN
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Keynote Speakers
大会主旨发言人

Keynote I

Dogma, Paradigm Shifts, and Recurring and Emerging Themes in the Cancer Field

Tuesday, Oct. 16
8:20 - 9 a.m.
BSRB Kahn Auditorium

Eric R. Fearon, MD, PhD
Emanuel N. Maisel Professor of Oncology
Professor of Internal Medicine, Human Genetics and Pathology
Director, U-M Rogel Cancer Center

ABSTRACT: Over the past fifty years, there has been remarkable progress in biological sciences and in medicine in general. Arguably, laboratory, clinical, and population science research advances in the cancer field have been as significant as in any area of disease-oriented research. Among other achievements in the cancer field, there has been outstanding progress in defining the role of selected genetic and epigenetic defects in key cellular factors and signaling networks in the genesis of cancers, as well as how some of the recurrent molecular defects in cancer cells underlie aberrant cancer-associated phenotypes. There has also been major progress in linking certain exposures, such as particular viruses and exogenous agents like tobacco products and ultraviolet light, to the origins of cancer as well as to effective cancer prevention and control approaches. Moreover, tremendous overall progress has been achieved with hormonal approaches, conventional chemotherapy and molecularly targeted agents, and most recently with immune- and cell-based approaches for the increasingly successful treatment of a number of different cancer types. Nonetheless, much work remains to increase the number of cures and improve the quality of life for all cancer patients and survivors, as well as to prevent cancers in high risk groups and the population at large. The presentation will comment on how dogma in the cancer field can limit innovation and progress, highlighting the importance of challenging and shifting paradigms for further progress. In addition, examples will be offered of how the intersection of selected recurring and emerging themes in cancer research leads to new research opportunities and directions for the cancer research field and new approaches to treat and prevent cancer.

BIOGRAPHY: Dr. Fearon received his medical and doctorate degrees from Johns Hopkins University before joining U-M in 1995 as Associate Director for Basic Science Research at the Rogel Cancer Center. His role within the Center expanded in 2005 to Deputy Director, and he was named Director in 2016. The Center is currently ranked 15th in the nation (and number one in Michigan) for cancer care by US News and World Report and is among just 49 cancer programs in the United States designated by the National Cancer Institute as a Comprehensive Cancer Center. Dr. Fearon has pursed research in the cancer genetics field, particularly investigations of selected gene defects that underlie colon and rectal tumor development and progression to advanced stages. The author of more than 135 peer-reviewed research manuscripts and more than 60 review/editorial articles and book chapters, Dr. Fearon has served on the editorial boards of various journals in the cancer biology and human genetics fields and currently is an editorial board member or editor for a number of journals, including *The Journal of Biological Chemistry*, *Current Biology*, *Journal of Clinical Investigation*, *Gastroenterology* and *Molecular Cancer Research*. In addition, he has served as a member or chair of various National Institutes of Health and National Cancer Institute advisory groups and grant review committees, including the Panel to Investigate the NIH Investment in Gene Therapy, the National Cancer Institute Board of Scientific Advisors, and the NIH Pathology B and Cancer Genetics Study Sections.

Keynote II

Precision Drug Therapy for Gastric Cancer: Current Status and Future Directions

Tuesday, Oct. 16
9-9:40 a.m.
BSRB Kahn Auditorium

Xiaotian Zhang, MD
Professor of Gastrointestinal Oncology
Peking University Cancer Hospital

ABSTRACT: In China, more than 70% of Gastric Cancer (GC) patients were diagnosed with advanced GC necessitating drug treatment. Trastuzumab was the only drug with a definite target suitable for 10-15% of HER2-positive GC patients. Due to the high heterogeneity of GC, it is urgent and challenging to explore the precision therapy for it. Future directions are as follows:

- Based on the clinical research cohort and PDX model, the prospective multi-center clinical trials and basic-translational research of targeted therapy will be carried out with the direction of clinical needs.
- According to both the efficacy and side effects from prospective clinical trials, the best combination of immunotherapy is optimized and the group who can benefit from immunotherapy is explored in vitro and in vivo.
- Based on large omics data of molecular typing, the molecules or pathways closely related to carcinogenesis / recurrence / metastasis, drug efficacy, and resistance are searched and validated, which will provide strong evidence for personalized therapy and subsequent new drug development.

BIOGRAPHY: Professor Xiaotian Zhang, MD, is Deputy Director of Teaching and Research for Medical Oncology. Her clinical and translational research focuses on issues in clinical practice, especially for advanced gastric cancer. She has participated in over a dozen international and domestic multi-center clinical trials. As the local PI, she is now leading implementation of several Phase II and III clinical trials on the first- and second-line treatment for gastric cancer. As the coordinator, she is in charge of the design, implementation, quality control and evaluation of a large-sample multi-center Phase III randomized trial (PACC of advanced gastric cancer) and two large-scale, domestic, multi-center Phase III randomized trials (RESOLVE and RESOLVE2) for locally advanced gastric cancer.

Keynote Speakers
大会主旨发言人

Keynote III

Strategic Research Planning and Priorities: Responding to Change and Securing the Future

Wednesday, Oct. 17
8:30-9:10 a.m.
BSRB Kahn Auditorium

Stephen Kunkel, PhD
Senior Associate Dean
for Research
Endowed Professor of
Pathology, UMMS

ABSTRACT: In order to support for the full spectrum of research activities, the University of Michigan Medical School has developed a robust strategic research plan. The strategy is based on the tenets that discovery of the right mechanism(s) via basic research, leads to the discovery of the right target through translational research, which results in the right therapy for our patients. This initiative, branded as "Fast Forward to Tomorrow's Cures," is bound together by three integrated parts: targeted innovative science, infrastructure to enable science broadly, and a research board of directors to provide leadership. Fast Forward is underpinned by four strategies: (i) capitalizing on the intersection of traditional research strengths to create new science at the boundary of old, (ii) leveraging the expertise in basic, clinical, and clinical trials research to impact our patients and improve health outcomes, (iii) building enterprise wide infrastructure to accelerate the pace of research, and (iv) developing our research workforce by retaining, recruiting, and creating a pipeline of talent. In order to enable more, better, and faster research, pillars of infrastructure have been established. These interactions resulted in the successful launch of multiple research enablers, including, but not limited to, a central biorepository, robust core facilities, research data warehouse (DataDirect), honest broker office, medical innovation initiative, "R01 Bootcamp", and a reinvigorated clinical trials system. The infrastructure for and enablers of research continue to provide the underpins for cutting-edge investigation. Thus, a number of near-term opportunities have become very viable. One in particular which is rapidly moving forward is the Precision Health Initiative, which capitalizes on the investments the Medical School has made in supporting infrastructure such as the central biorepository (CBR) and data warehouses. Presently, over 400,000 samples are contained in the CBR which is connected via bar codes to electronic health records in our data warehouses. A significant number of the banked specimens have been DNA sequenced, further supporting the Precision Heath Initiative. The process of planning and prioritizing research efforts is often challenging for large academic medical centers; however, it is an imperative activity for responding to change and securing our future.

BIOGRAPHY: As senior associate dean for research, Dr. Kunkel provides direction for the school's research mission, including setting goals for developing a major global presence for the Medical School's research enterprise. He received his PhD from the University of Kansas in microbiology and served his postdoctoral fellowship at the University of Connecticut Health Center. He joined the University of Michigan Medical School faculty in 1980. Dr. Kunkel's areas of research have centered on assessing molecular mechanisms of lung inflammation by investigating cytokine and chemokine directed cell-to-cell communication circuits. His studies in cytokine and chemokine biology are internationally recognized and have provided a clearer understanding of how these proteins participate in the initiation, maintenance, and resolution of acute and chronic lung. His research group has provided evidence for specific cytokine phenotypes that dictate the progression of particular chronic diseases. Dr. Kunkel has co-authored more than 600 peer-reviewed manuscripts, contributed more than 60 chapters to different books in his field, served as the editor for four books, presented 150-plus lectures as a visiting professor/lecturer in the past 10 years, and maintained continuous funding of multiple National Institute of Health grants for a number of years, including the principal investigator of a program project to study lung inflammation. He is the recipient of a previous NIH MERIT Award, served on National Institute of Health peer review study sections, organized numerous international conferences on inflammation, and is an associate editor for various professional scientific journals. He is the present co-chair of the Board of Scientific Counselors for the NIAID-NIH.

Keynote IV

Strategic Research Planning at PKUHSC

Wednesday, Oct. 17
9:10-9:50 a.m.
BSRB Kahn Auditorium

Ning Zhang, PhD
Professor of Oncology
Vice President, Peking University Health Science Center

ABSTRACT: As the most prestigious comprehensive medical institution in China, Peking University Health Science Center (PKUHSC) developed out of National Medical School of Peking, the first national school of western medicine established by the Chinese government through its own efforts. Since its inception in 1912, PKUHSC has cultivated a large number of high-level medical and health talents for the country, and has made outstanding contributions to improving the health of the Chinese people

Currently, PKUHSC has five on-campus academic schools and 10 affiliated hospitals. With the historic opportunities that the national rejuvenation and the Healthy China 2030 Initiative stand to offer, PKUHSC is committed to its responsibilities to the nation. In recent years, PKUHSC has made substantial progress in education, research, patient care, and healthcare system innovation on multiple fronts. In research, PKUHSC has experienced rapid development in biomedical research, especially in fields like cardiovascular disease, cancer and hematological disease, reproductive and regenerative medicine, neuroscience and clinical psychiatry, orthopaedics and sports medicine, immunology and rheumatic disease, urology and nephrology, and dentistry.

In 2016, the Chinese government launched the Healthy China 2030 Initiative and then in 2017 the National Double First-Class Initiative, in which advancing medicine plays an important role. As a prestigious higher education institution in China, Peking University has an unshakable responsibility to lead researches and education in medicine and health sciences and contribute its share to implementing these two initiatives. To achieve this goal, the plan "Peking University Medicine" has been put forward by PKUHSC with the aim to break the boundaries between schools and disciplines within Peking University; to pool resources of all medically-related disciplines at PKU; to integrate medicine with engineering, science, optics, electronics, material science, nanotechnology, bioinformatics, big data and etc. To implement "PKU Medicine", Med X Program, which means integrated development of multiple disciplines with medicine at the core, is a key strategy. Med X Program is the only scientific research program endorsed at the university level and supported by over 15% of the university's total budget. PKUHSC has just started to implement the program. We have established several research centers with faculties from various disciplines, including the National Center for Health Big Data, the Center for Biomedical Engineering, and the Center for Chemical Biology. Meanwhile, the university has established several research funds to support the collaboration between clinician scientists from the university hospitals and researchers from other disciplines on the campus.

International collaboration also plays an important role in our strategic research planning. PKUHSC's international research collaboration platform has just been awarded "International Collaboration Center for Translational and Clinical Research" by the Ministry of Science and Technology, PRC. And PKUHSC-Michigan Medicine Joint Institute certainly plays a very important role in this new center. With joint efforts with our partners, we hope to achieve great things in medicine and health that one cannot achieve alone.

BIOGRAPHY: Dr. Ning Zhang currently serves as the Vice President of Peking University Health Science Center and has been engaged in biomedical and cell biology research for many years. Focused on tumor metastasis, his research involves mechanism study, biomarker identification, drug screening, and the application of nanotechnology. Dr. Zhang has received many awards for his achievement in cancer research, including Young Science and Technology Innovation Talents from the Ministry of Science and Technology, Distinguished Young Scholar Awards from Nature Science Foundation, Chief Scientist of National Program on Key Basic Research Project (973), New Century Excellent Talents from Ministry of Education, Distinguished Professor of Tianjin, and Excellent Achievement Award from Lee's Foundation.

Overview of Joint Institute Programs and Cores

联合研究所研究项目与核心支撑平台简介

The Joint Institute has four established research programs: **Cardiovascular Disease, Liver Disease, Pulmonary Disease,** and **Renal Disease**. Each of these program areas were chosen because of their overall importance to global health, as well as the opportunity for effective collaboration and the potential for translational impact.

Overview of Joint Institute Programs and Cores
联合研究所研究项目与核心支撑平台简介

Leads

Eugene Chen, MD, PhD
Frederick G.L. Huetwell Professor of Cardiovascular Medicine
UMMS

David J. Pinsky, MD
Chief of Cardiovascular Medicine, UMMS

Wei Gao, MD, PhD
Professor and Chief of Cardiology
PKUHSC Third Hospital

Jianping Li, MD, PhD
Professor, Executive Deputy Director
Department of Cardiology
PKU First Hospital

Cardiovascular Disease Program

Cardiovascular disease takes the lives of more than 16.7 million people (29.2 percent of total global deaths) each year and at least 20 million others suffer heart attacks or strokes according to World Health Report 2003. While significant strides have been made in the prevention and treatment of cardiovascular disease, there is still much the scientific community does not understand about how it develops.

The partnership between UMHS and PKUHSC offers a unique opportunity for leading researchers to study the disease in a large, genetically diverse patient population. Thus the Joint Institute has initiated several important studies designed to significantly advance understanding about the genetic basis of cardiovascular disease.

In particular, the Joint Institute's work in this area studies the role genetics play in the development of risk factors, such as high blood pressure, as well as in the onset of cardiovascular diseases, including myocardial infarction, abdominal aortic aneurysm, and coronary artery disease. In addition, scientists are systematically studying the genetics and biology related to high-density lipoprotein (HDL), or "good," cholesterol to identify new strategies for effectively raising HDL in patients.

Active Cardiovascular Projects

Molecular Mechanisms of Fibrosis and the Progression from Paroxysmal to Persistent Atrial Fibrillation

UMMS Lead: Jose Jalife PKUHSC Lead: Xuebin Li

The Role of Hematopoietic Factors in Atherosclerotic Vascular Diseases

UMMS Lead: Santhi Ganesh PKUHSC Lead: Yan Zhang

Multi-ethnic Study of Genetic Risk Factors to Discover Mechanisms of Aortic Aneurysm and Dissection

UMMS Lead: Cristen J. Willer PKUHSC Lead: Zhe Zhang

Evaluation of SpironolactoNe Versus Indapamide on Target Organ Damage in Patients with Obesity and Hypertension (ENVOY)

UMMS Lead: Bertram Pitt PKUHSC Lead: Guisong Wang

Overcoming Racial Disparity in Antiplatelet Therapy

UMMS Lead: Daniel Eitzman PKUHSC Lead: Jianping Li

β-adrenergic Receptor Activation in Cardiac Injury and Atherosclerotic Plaque Stability: Role of NPDPH Oxidase 4

UMMS Lead: Marschall Runge PKUHSC Lead: You-Yi Zhang

Closed Projects

Dysfunctional HDL and Cardiovascular Disease

Finding Genes for Myocardial Infarction and Blood Lipid Levels in a Chinese Sample from Beijing

Blood Pressure and Hypertension Genetics

Particulate Matter Air Pollution and High Density Lipoprotein Dysfunction

Identify Smooth Muscle Cell Specific Protein as Biomarkers for Early Diagnosis of Acute Aortic Dissection

Quantitative Measurements of Brain Iron Overload after Intracerebral Hemorrhage

A Chemical Approach to Generating Patient-specific Cardiac Stem Cells for Cell Therapy Against Cardiovascular Disease

JI Awards To Date: 13

Completed Projects: 7

Samples Under Study: 19k

Publications To Date: 30

Extramural Funding: $6.8m

Overview of Joint Institute Programs and Cores
联合研究所研究项目与核心支撑平台简介

Leads

Chung Owyang, MD
H. Marvin Pollard Collegiate Professor of Internal Medicine
Division Chief, Gastroenterology
Director, Digestive Health Center, UMMS

Anna S. Lok, MD
Alice Lohrman Andrews Research Professor of Hepatology
Assistant Dean for Clinical Research, UMMS

Lai Wei, MD, PhD
Professor and Director
Peking University Hepatology Institute
PKU Second Hospital

GI & Liver Disease Program

While much progress has been made in the treatment and prevention of liver diseases, viral hepatitis (B and C), fatty liver disease, and liver cancer continue to pose a significant health threat worldwide, and are of special concern in Asia — the world's most populous continent. The unique partnership established by the Joint Institute provides scientists at UMHS and PKUHSC an unprecedented opportunity to study liver diseases in large, genetically diverse patient populations and undertake rigorous, translational research that significantly improves patient care. The Joint Institute's support of GI/Liver Diseases Program has expanded over the years from one initial study on hepatitis C to now include four studies.

Active GI/Liver Projects

Role of Visceral Adiposity in the Pathogenesis of Non-Alcoholic Fatty Liver Disease in Lean Versus Obese Patients: A Comparative Study between Patients at UMHS versus PKUHSC

UMMS Lead: Anna Lok PKUHSC Lead: Lai Wei

Image-Guided Surgery of Hepatocellular Carcinoma

UMMS Lead: Tom Wang PKUHSC Lead: Jiye Zhu

Identification of Tumoricidal T Cell Receptors from Hepatocellular Carcinoma-infiltrating CD8+ T Lymphocytes

UMMS Lead: Clifford Cho PKUHSC Lead: Yuan Hong

Systematic Investigation of the Microbiome-host Interactions in H. pylori-associated Gastric Cancer Patients

UMMS Lead: Yongqun He PKUHSC Lead: Jianmin Wu

Closed Projects

Predictors of Hepatitis C Progression

Genomic Evolution and Mutational Signature of Esophageal Cancer in Anyang, China

Effects of Diet and Genetic Factors on Gut Gysbiosis in IBS

JI Awards To Date: 7

Completed Projects: 3

Patients Under Study: 2700

Publications To Date: 15

Extramural Funding: $4.9m

Overview of Joint Institute Programs and Cores
联合研究所研究项目与核心支撑平台简介

Co-Leads

Theodore Standiford, MD
Henry Sewall Professor of Medicine
Division Chief, Pulmonary & Critical Care Medicine
UMMS

Bei He, MD, HCCP, ERS
Director
Pulmonary Division
PKU Third Hospital

Pulmonary Disease Program

According to joint research published by the World Health Organization and the World Bank, chronic obstructive pulmonary disease (COPD) is projected to rank fifth in global burden of disease by the year 2020. Despite significant progress in the study and treatment of COPD — as well as public health initiatives to reduce tobacco consumption — COPD, and its related complications, continue to pose serious and significant health threats to people worldwide, involving both industrialized and developing nations.

The Joint Institute's work focuses on building a new area of COPD research investigating the role that the respiratory microbiome plays in the development and clinical course of lung disease, specifically COPD. Once discounted as unimportant, new scientific evidence suggests that the composition of the microbiome, both respiratory and gastrointestinal, has profound effects on multiple aspects of human health including immune and inflammatory responses.

The research partnership between UMHS and PKUHSC offers a unique opportunity to study the respiratory microbiome in large and genetically diverse patient populations. Aided by recent technological advances in microbial genomic sequencing, the Joint Institute's Pulmonary Disease Program is initiating several studies in this new and exciting field.

Active Pulmonary Projects

DNA Methylation Changes Induced by Air Pollution Contributes to Chronic Airway Inflammation and Airway Remodeling in Moderate-to-Severe Uncontrolled Asthma

UMMS Lead: Steven Huang PKUHSC Lead: Yahong Chen

Compartmental Analysis of Metabolite Profiles Associated with Disease Phenotypes in Chinese and US Smokers with and without COPD

UMMS Lead: Theodore Standiford PKUHSC Lead: Bei He

Rapid Identification of Pathogens in Ventilator-associated Pneumonia using Real-time Metagenomics and Real-time PCR

UMMS Lead: Robert Dickson PKUHSC Lead: Ning Shen

Therapeutic Implications of Natural Killer Cell Immune Surveillance in Lung Cancer

UMMS Lead: Venkateshwar Keshamouni PKUHSC Lead: Jun Wang

Targeting Tumor Neoantigen-specific Tumor Infiltrating Lymphocytes in Non-small Cell Lung Cancer

UMMS Lead: Andrew Chang PKUHSC Lead: Jixian Lu

Closed Projects

Analysis of the Microbiome in Smokers without COPD and with COPD: Comparisons Between US and Chinese Populations

Overview of Joint Institute Programs and Cores
联合研究所研究项目与核心支撑平台简介

Co-Leads

Matthias Kretzler, MD
Warner-Lambert/Parke-Davis Professor Medicine, Professor of Internal Medicine, Nephrology Computational Medicine & Bioinformatics, UMMS

Wenjun Ju, PhD
Associate Research Scientist
Department of Internal Medicine, UMMS

Minghui Zhao, MD, PhD
Professor of Medicine
Chief of Renal Division
PKU First Hospital

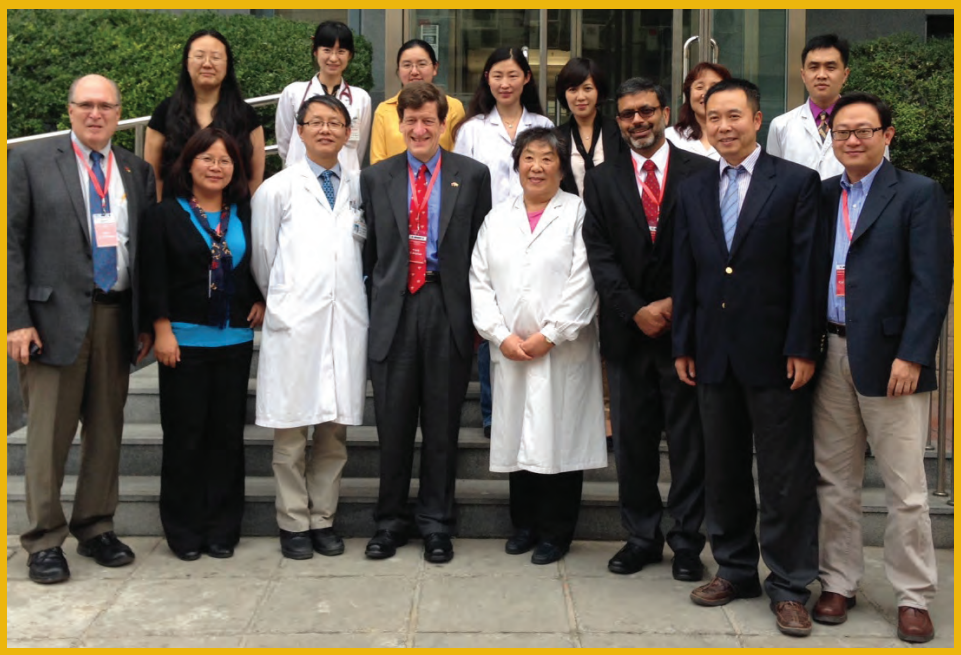
Hong Zhang, MD, PhD
Professor of Medicine
Renal Division, PKU First Hospital
PKU Institute of Nephrology

Renal Disease Program

Patients with end-stage renal disease (ESRD) require renal replacement therapy associated with high morbidity, mortality and cost both in China and the US. The majority of ESRD originates from glomerular disease.

The UMHS and PKUHSC renal divisions play a leading role in translational chronic kidney disease (CKD) research in US and China. We are committed to solving the most urgent unmet needs in this field, including the early and accurate identification of patients at high risk of progressing to end-stage kidney disease, the need for early and targeted treatments for these high risk patients. The joint scientific expertise, unique resources (biobanks established by both divisions host urine and plasma samples accumulated over years from patients with glomerular diseases, these samples are linked with longitudinal clinical data), and the deep trust-based intensive cooperation and exchanges (including faculty training, multiple visits, shared seminars etc.) position us strongly to meet this challenge. Together, we strive to (1) better understand the CKD prevalence, risk factors, and outcomes between China and the US; (2) develop non-invasive molecular markers for early detection of patients at high risk for progression to allow preventative management of CKD; and (3) identify molecular mechanisms driving glomerular disease progression as targets for interventional trials.

The JI renal program provides a valuable platform to exchange research ideas and to nurture new collaborations on renal diseases. We continue to welcome new projects and new investigators to the program. We strongly believe that our joint effort will contribute to improve patient care and reduce financial burden in both US and China.



Active Renal Projects

Identification of Shared and Specific Marker Panels for Diabetic Kidney Disease Progression

UMMS Lead: Wenjun Ju PKUHSC Lead: Ming Chen

Defining Molecular Mechanisms and Biomarkers for Progressive Renal End Organ Damage in Vasculitis

UMMS Lead: Matthias Kretzler PKUHSC Lead: Minghui Zhao

Mitochondrial Nutrient Metabolism and Progression of Chronic Kidney Disease

UMMS Lead: Subramaniam Pennathur PKUHSC Lead: Nan Hu

Closed Projects

Towards Molecular Prognosis of Chronic Kidney Disease (CKD) in UMMS and PKUHSC

Comparison of Chronic Kidney Disease (CKD) Prevalence, Risk Factors and Outcomes between China and the United States

Urine Protein Glycosylation and Progression of Chronic Kidney Disease

Prevention of Kidney Failure in Alport Syndrome by Application of Podometric Technology

JI Awards To Date: 7

Completed Projects: 4

Patients Under Study: 9k

Publications To Date: 9

Extramural Funding: $1.6m

Other Exploratory Projects

In addition to the initial four fields of research (i.e. Cardiovascular, GI/Liver, Pulmonary, and Renal diseases), the JI is increasingly invested in collaborations spanning other areas of practice. While the exploratory program is young, the number of projects is expanding rapidly, with ten awards over the last three years in disciplines including Emergency Medicine, Psychiatry, Obstetrics and Gynecology, and more. These projects already have more than 5,400 patients and/or samples under study and have yielded 6 publications to date.

Active Exploratory Projects

Imaging Biomarkers for Staging and Assessing Response to Therapy in Multiple Myeloma

UMMS Lead: Qian Dong PKUHSC Lead: Jin Lu

Epigenetic Effects of Prenatal Environment Exposures

UMMS Lead: Margit Burmeister PKUHSC Lead: Ming Li

Targeting Peptidylarginine Deiminase (PAD) for Diagnosis and Treatment of Severe Inflammation

UMMS Lead: Hasan Alam PKUHSC Lead: Baoguo Jiang

Active Exploratory Projects, *cont.*

Risk-Adjusted Outcome Prediction Tool for Emergency Department Intensive Care Unit Patients
UMMS Lead: Kyle Gunnerson PKUHSC Lead: Qingbian Ma

Building Collaborations to Address Drug Problems in the United States and China
UMMS Lead: Frederic Blow PKUHSC Lead: Lin Lu

Understanding the Role of Potassium Channel Gene Mutations in Pediatric Epilepsy
UMMS Lead: Lori Isom PKUHSC Lead: Yuwu Jiang

Human Embryo Mosaicism Influence on Preimplantation Genetic Screening (PGS), Embryo Development, and Human Embryonic Stem Cell (hESC) Development and Genetic Stability
UMMS Lead: Gary Smith PKUHSC Lead: Jie Qiao

Longitudinal Assessment of Cartilage Injury and Remodeling After Anterior Cruciate Ligament Rupture and Reconstruction: A Correlational Study of Functional Imaging and Biomarkers
UMMS Leads: Asheesh Bedi & Tristan Maerz PKUHSC Lead: Yingfang Ao

Rapid Bacterial Identification and Antibiotic Susceptibility Testing in Patients with Sepsis by CD NR-PCR
UMMS Lead: Scott VanEpps PKUHSC Lead: Yaan Zheng

Integrative and Trans-ethnic Cutaneous T-cell Lymphoma (CTCL) Study to Reveal Clinical and Molecular Determinants for Disease Prognosis
UMMS Lead: Lam Tsoi PKUHSC Lead: Yang Wang

Understanding the Heterogeneity in the Risk of Diabetes Complications in China and the US
UMMS Lead: Rodica Pop-Busui PKUHSC Lead: Luxia Zhang

Identification and Establishment of Novel Pathogenic Genes Involved in Intellectual Disability/ Developmental Delay with Hypomyelinating Leukodystrophy in China
UMMS Lead: Margit Burmeister PKUHSC Lead: Jingmin Wang

Disciplines

Obstetrics & Gynecology
Radiology
Psychiatry
Surgery
Emergency Medicine
Pharmacology
Orthopaedics
Oncology
Endocrinology

JI Awards To Date: 10

Extramural Funding: $185k

Publications To Date: 6

Overview of Joint Institute Programs and Cores
联合研究所研究项目与核心支撑平台简介

Research Cores

The Joint Institute's Research Cores facilitate the critical work of each of the four research program areas and include the Biorepository and Biomedical Informatics Core, the Collaboration Core, and the Institutional Review Board and Human Protection Core.

Each of these cores are designed to support productive collaboration by establishing the technological infrastructure and administrative assistance needed for success, and by providing joint oversight to ensure the work adheres to established standards and practices for research involving human subjects and tissue.

Leads: *Biorepository Core*

Kai Zheng, PhD
Associate Professor
Department of Informatics
Co-Director, Center for Biomedical Informatics
University of California, Irvine

Yanfang Wang
MD, PhD, MS, MHSc
Professor and Associate Director Peking University Clinical Research Institute
PKUHSC

Fan Meng, PhD
Research Associate Professor of Psychiatry
Molecular and Behavioral Neuroscience Institute, UMMS

Biorepository/Biomedical Informatics Core

The Biorepository and Biomedical Informatics (BRBI) Core is responsible for establishing standardized procedures for the acquisition, storage, and management of biospecimens and data that support the Joint Institute's research missions. The BRBI Core provides a robust electronic data capture infrastructure to support field data entry and sharing and long-term management of the data. It also strives to provide project management support such as patient consent and sample tracking, allowing investigator teams to focus on their core research tasks. All Joint Institute programs and investigators are required to follow the standards established by this core.

Leads: *IRB Core*

Raymond Hutchinson
MS, MD
Associate Dean for Regulatory Affairs
Professor of Pediatrics & Communicable Diseases, UMMS

Yali Cong, PhD
Professor of Medical Ethics, PKUHSC

Michael Geisser, PhD
Professor of Physical Medicine & Rehabilitaiton
UMMS

Institutional Review Board & Human Protection Core

The central mission of the Joint Institute's Institutional Review Board (IRB) and Human Protection Core is to promote the protection of human participants in the research being conducted by the Joint Institute. The Board comprises representatives from the internal IRBs of both universities. Through careful review and monitoring of Joint Institute Programs and proposals, the Board works to ensure that research activities adhere to all applicable laws, regulations, and institutional policies for research involving human subjects. The Joint Institute IRB serves as liaison to the Michigan Medicine IRBMED and the PKUHSC IRB ensuring that all collaborations meet the human protection standards in place at both universities.

Overview of Joint Institute Programs and Cores
联合研究所研究项目与核心支撑平台简介

Collaboration Core

The Collaboration Core was established to facilitate a genuine partnership between the University of Michigan Health System and Peking University Health Science Center. The Collaboration Core conducts research into the science of collaboration. It tracks the collaboration needs and goals of each institution, defines success measures, and identifies the management structures and processes that lead to favorable outcomes. By conducting and publishing this research, the Collaboration Core furthers the science of collaboration, sheds light on the social and technical practices that facilitate effective collaborations, and helps develop knowledge about how to build and facilitate effective partnerships.

Based on its research, the Collaboration Core assists the Joint Institute management teams to formulate strategies related to communication, project management, and coordination by providing advice and guidance to the program and management teams and coordinating with the Biorepository/Biomedical core to build the technical infrastructure necessary to support collaboration. This important function touches virtually every facet of the Joint Institute and serves as a central "hub" of information for research conducted by the program scientists.

Leads: *Collaboration Core*

Amy Huang, MD, MHSA
Director for China Programs
Global REACH
Adjunct Assistant Professor
Cardiovascular Medicine
Department of Internal Medicine
UMMS

Qiudan Sun, MA
Professor and Director
Office of International Cooperation
Associate Director, Institute of Medical Education
PKUHSC

New Joint Institute Projects
联合研究所新资助课题

New projects for 2018

Ten new research projects have been selected for the most recent round of funding through Michigan Medicine's Joint Institute partnership with Peking University Health Science Center. The projects, each co-led by a UMMS faculty member and their PKUHSC partner, span a number of disciplines from pulmonary medicine and cardiology to diabetes complications and cognitive disabilities research. Congratulations to all of the recipients.

Identification of Tumoricidal T Cell Receptors from Hepatocellular Carcinoma-infiltrating CD8+ T Lymphocytes

Hepatocellular carcinoma (HCC) is an aggressive malignancy whose poor prognosis is driven in part by a lack of curative treatment options. We previously cloned three novel HCC-specific murine T cell receptor (TCR) genes that can redirect human T cells to effectively eliminate HCC tumor cells, demonstrating the potential to engineer a patient's autologous T cells to treat HCC. In addition, we have isolated specific CD8+ tumor infiltrating lymphocytes (TILs) from HCC patients and observed their potent antitumor function after in vitro proliferation. In this project, we seek to infuse CD8+ TILs derived from HCC patients into immunodeficient mice harboring autologous HCC, and subsequently clone TCR genes from patient-derived CD8+ T cells with antitumor phenotype. Following validation of their functions, we will determine their targeted tumor antigens through epitope prediction algorithms and unbiased screening using yeast-display libraries. In sum, we will identify novel tumoricidal TCR genes from HCC CD8+ TILs, thereby engineering patient-derived autologous T cells to generate potently tumoricidal TCR-T lymphocytes to treat HCC patients.

Co-Investigators

Clifford Cho, MD, FACS
C. Gardner Child Professor of Surgery
Chief, Division of Hepato-Pancreato-Biliary and Advanced GI Surgery, UMMS

Yuan Hong, MD, PhD
Associate Researcher
Liver Diseases Center
Peking University First Hospital

Therapeutic Implications of Natural Killer Cell Immune Surveillance in Lung Cancer

Brief background: Lung cancer is the leading cause of cancer mortality worldwide. Use of immune-checkpoint blockers has yielded impressive clinical benefit, but only in a subset of patients. Recent studies demonstrate that the expression of the checkpoint-ligands like PDL-1 on host cells, rather than on cancer cells, determines the efficacy of checkpoint-blockade in mice. A number of host immune cells, including NK cells, express PDL-1 and could dictate the efficacy of checkpoint-inhibitors in humans. A recent phase I/II study combining anti-KIR (an inhibitory NK cell receptor) antibody with anti-PD1 antibody in head & neck cancer showed a dramatic 24% objective response rate over 13.3% with anti-PD1 alone. Epithelial-mesenchymal transition (EMT) is a transdifferentiation process by which epithelial cancer cells acquire migratory

Co-Investigators

Venkateshwar Keshamouni, PhD
Associate Professor of Pulmonary & Critical Care, UMMS

Jun Wang, MD, PhD
Professor of Thoracic Surgery
Peking University Second Hospital

and invasive capabilities to metastasize. We demonstrated that a 20-gene EMT-signature is predictive of survival in non-small cell lung cancer (NSCLC) patients. More recently, we showed that EMT-induced expression of a cell-adhesion molecule CADM1 renders cancer cells more susceptible to NK cytotoxicity and inhibits metastasis. This proposal will test whether boosting NK cell functions can control metastasis and whether the EMT signature can be predictive of anti-tumor efficacy of NK cell therapy, as well as response to checkpoint-blockade therapy in NSCLC.

Specific aims: 1) Test the efficacy of NK cell-based strategies, including adoptive transfer of NK cells, in inhibiting tumor progression, using PDX models of NSCLC in NSG mice. 2) Determine whether EMT-signature and NK cell phenotype in blood and /or primary tumor predict benefit from NK cell therapy and response to checkpoint-blockade.

Expected outcomes: These studies will provide proof-of-principle for a potential phase I/II study for proposed NK cell-based strategies, along with the support to the potential of EMT-signature and NK cell phenotype in predicting response to checkpoint-blockade and pave the way for subsequent mechanistic studies.

Rapid Identification of Pathogens in Ventilator-associated Pneumonia Using Real-time Metagenomics and Real-time PCR

Background and importance: Ventilator-associated pneumonia (VAP) is a tremendous cause of morbidity, mortality, and healthcare expense in China and the United States. Clinical identification of respiratory pathogens still relies on the culture-based techniques used by Pasteur in the 1880s. Delayed identification of pathogens in pneumonia results in increased morbidity and mortality, and indiscriminate use of broad empiric antibiotics impedes antimicrobial stewardship. This novel study will extend recent discoveries in molecular microbiology to the rapid detection of pathogens in VAP.

Long-term objectives: The long-term objective of this proposal is to accelerate the identification and quantification of pathogens in VAP using novel, real-time molecular technologies. In Objective 1, we will develop a

Co-Investigators

Robert Dickson, MD
Assistant Professor of Internal Medicine, UMMS

Ning Shen, MD
Chief Physician of Respiratory Medicine
Peking University Third Hospital

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联合研究所新资助课题

protocol and pipeline that will rapidly identify respiratory pathogens in four hours via real-time metagenomics. In Objective 2, we will develop a protocol and determine reference ranges that will rapidly quantify respiratory pathogens in two hours using a novel ultrasensitive PCR platform.

Integrative and Trans-ethnic Cutaneous T-cell Lymphoma (CTCL) Study to Reveal Clinical and Molecular Determinants for Disease Prognosis

Cutaneous T-cell lymphoma (CTCL) is a major form of the primary cutaneous lymphomas and affects all populations in the world including the American and Chinese. CTCL symptoms range from mild itchy red patches to large, painful, disfiguring, cerated nodules, and patients with the advanced stages of CTCL only have up to a 50% three-year survival rate. CTCL patients respond differently to current available treatments, and the subtypes (e.g., Sézary syndrome) vary greatly in their relapse-rate and prognosis. While we and others have conducted population-specific genetic, epidemiological, and/or molecular studies, there has not been any cross-ethnic study to systematically evaluate the shared/unique risk factors associated with prognosis cross populations. With CTCL being an uncommon cancer with limited armamentarium in management, it is imminent to identify robust prognosis biomarkers. This project will set forth the first collaboration between the Michigan Medicine Department of Dermatology and the PKUHSC Department of Dermatology, as well as Venereology from the Peking University First Hospital, drawing on the unique resources and the expertise of the investigators from the two institutions. First, we have a large Chinese CTCL cohort in PKUHSC with records and/or samples from >600 patients. Second, UMHS and the Dermatology clinics have access to >1,400 CTCL patients medical records, and we also banked the biopsies with various immunophenotypes of these patients. Thirdly, we have vast experience in statistical and omics analysis for assessing disease outcomes, including in-house bioinformatics pipelines developed in the Michigan Medicine Center for Cutaneous Bioinformatics.

Co-Investigators

Lam Tsoi, PhD
Research Assistant Professor
Dermatology, UMMS
Computational Medicine & Bioinformatics, UMMS

Trilokraj Tejasvi, MBBS, MD
Assistant Professor of Dermatology, UMMS

Yang Wang, MD
Associate Professor of Dermatology and Venereology
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β-adrenergic Receptor Activation in Cardiac Injury and Atherosclerotic Plaque Stability: Role of NPDPH Oxidase 4 (NOX4)

Cardiovascular disease (CVD) is the leading cause of death worldwide, representing 31% of all deaths. Emerging evidence suggests that stress in adulthood acts as a disease trigger in individuals with high atherosclerotic burden and is a determinant of prognosis and clinical outcomes. Increases in cardiovascular events were reported immediately after traumatic events such as natural disasters, war, and terrorist attacks of 9-11. Although the link between various stressors and disease end points is obvious, much less is known about the pathophysiological mechanisms through which stress responses transform into changes that initiate the development and progression of CVD. Another challenge is addressing the stressors by intervention, because such events are stochastic and therefore difficult to predict. We propose to elucidate the molecular signaling pathways which regulate the transformation of stress responses into cardiovascular events in people with atherosclerotic burden using mouse models of oxidative stress available in the Runge laboratory. Our proposal has three innovative aspects. First, our team has complementary strengths required for investigating the effect of sympathetic adrenergic activation on the onset of cardiovascular events in the backdrop of high atherosclerotic burden. Second, we generated atherosclerosis data using novel Apoe-/-/mNox4TG mice and Apoe-/-/Nox4-/- mice. Third, we plan to evaluate the effect of metformin and GKT137831 on β-AR activation associated cardiac dysfunction in mNox4TG mice and atherosclerotic burden and plaque stability in Apoe-/-/mNox4TG mice. Our research strategy includes the following two specific aims: (1) determine the molecular mechanism of sympathetic activation induced cardiac inflammatory injuries in mice deficient in and with mitochondrial-specific overexpression of Nox4; (2) investigate the mechanisms of β-AR induced atherosclerotic burden/plaque instability in Apoe-/- mice deficient in and with mitochondrialspecific overexpression of Nox4. Together, these studies will establish the role of NOX4 NADPH oxidase in cardiovascular events in the backdrop of high atherosclerotic burden and potentially identify strategies that work in concert with standard of care treatment for the prevention of cardiovascular events under stress conditions.

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Targeting Tumor Neoantigen-specific Tumor Infiltrating Lymphocytes in Non-small Cell Lung Cancer

Tumor infiltrating lymphocytes (TILs) comprise a subset of white blood cells isolated from the tumor and surrounding parenchyma that are thought to mediate tumor-specific immune responses. Autologous TIL cultures, isolated from resected tumor tissue, expanded ex vivo and subsequently reinfused into the preconditioned donor patient, have been shown to elicit durable response rates with some instances of long-term survival. In contrast, another subset of TILs appears to attenuate clinical response. We hypothesize that TILs which recognize tumor-specific neoantigens originate from somatic mutations and are more effective in eliciting a clinically significant response. As proof of concept, it has been shown that TILs harvested from resected metastatic lung tumors from a subject with metastatic colorectal carcinoma recognized neoantigens generated by the mutant KRAS-G12D. Re-infusion of expanded TILs led to a significant antitumor response in this subject. The aim of our study is to utilize high throughput sequencing and tetramer flow cytometry to identify tumor-specific neoantigens derived from patients with non-small cell lung carcinoma, both adenocarcinomas and squamous cell carcinomas, as a prelude to the treatment of NSCLC patients with autologous T cells.

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Understanding the Heterogeneity in the Risk of Diabetes Complications in China and the US

The global trend towards obesity, physical inactivity and energy-dense diets has led to a rapid rise in the prevalence of diabetes. It is estimated that 415 million people live with diabetes, with a projected increase to 642 million by 2040. Practical and cost-effective interventions at national levels are essential to attenuate the global burden of diabetes. Current evidence have shown that glucose control designed to achieve near-normal glycemia may reduce the risk of chronic complications in patients with type 1 diabetes (T1D) and some patients with type 2 diabetes (T2D). However, a critical knowledge gap remains in understanding what persons with diabetes do or do not develop complications, independently of glucose control, and whether there are populations and regions-specific differences in this risk. We hypothesize that populations from different ethnic origin/regions express diverse specific phenotypes of diabetes and its complications. Understanding the heterogeneity in the

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risk for diabetes complications could enrich the knowledge of the pathophysiologic pathways, help to identify the high-risk population, as well as develop target intervention strategies for primary and secondary prevention of diabetes. The specific objectives are to understand the heterogeneity in the phenotype of chronic diabetes complications among patients with diabetes in the two nations, including (a) describing differences in phenotypes and patterns of long-term complications between two countries; and (b) unveiling clinical and biological biomarkers and using deep learning systems and precision medicine approaches to identify increased risk and/or protection from complications among Chinese and US populations. By tracking the adverse outcomes, we hope to identify mechanism-based therapies for the treatment of diabetes complications so treatment can be individualized and targeted appropriately.

Identification and Establishment of Novel Pathogenic Genes Involved in Intellectual Disability/ Developmental Delay with Hypomyelinating Leukodystrophy in China

Intellectual disability/development delay (ID/DD) is a common group of neurodevelopmental disorders characterized by substantial limitations in both intellectual functioning and adaptive behavior, starting before the age of 18 years with a prevalence of 1%~3%. Genetics is known to have an important role in etiology of ID/DD. Discerning the precise genetic causes for specific ID/DD patients will inform prognosis, management and therapy, enables access to disorder-specific support groups, and facilitates family planning. Specific knowledge of the genetic basis of disease may in some cases also lead to direct therapeutic interventions. Trio-based whole exome sequencing (WES) has become the best option to identify genetic causes of ID/DD. Although rare variants in more of >700 different genes have now been shown to be associated with ID/DD, many disease-causing genes still remain to be discovered. The respective research teams have already collaborated on genetic analysis of trio-based WES results of 20 families with ID/DD & hypomyelination leukodystrophy (HLD). Eight candidate novel genes related to ID/DD&HLD have been identified. Of these, TMEM106B, has just been published in *Brain*, and follow-up is underway on two other strong candidates: CSMD3 and TMEM63A. These preliminary data strongly support our overarching goal of this project: to identify and further study genetic causes of ID/DD&HLD patients. First, we propose to discover novel disease-causing genes through trio-based WES of 50 Chinese ID/

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DD&HLD families in whom there is a high clinical suspicion for an underlying genetic disorder. Our approach will benefit from prior collaboration of the two teams on HLD, a more specific sub-phenotype within the ID/DD spectrum. Second, taking advantage of the candidate novel genes identified through in prior collaboration, the mutation effect of candidate variants will be evaluated in patient-derived skin fibroblasts and in CRISPR/Cas9-edited human embryonic stem cell already transgenic for neurogenin2 (Ngn2), allowing use of a newly developed rapid neurogenesis method by forced expression of Ngn2 in stem cells (SCs), in cooperation with U-M's Human Stem Cell and Genome Editing core facility. Establishing neuronal cell lines for promising candidate gene variants will provide a cellar platform for pathogenesis studies and in-vitro drug screens.

Systematic Investigation of the Microbiome-host Interactions in H. pylori-associated Gastric Cancer Patients

Background: Gastric cancer is the fifth most prevalent malignancy and the third leading cause of cancer death worldwide. Almost a half of new cases of gastric cancer occurred in China, where it is the second leading cause of cancer death. The strongest risk factor for gastric cancer is chronic Helicobacter pylori infection. People with H. pylori infection have a roughly six-fold greater risk of developing gastric cancer than uninfected people. However, not all people infected with H. pylori will develop gastric cancer, suggesting more factors and mechanisms involved in gastric carcinogenesis. We hypothesize that complex interactions between host genetic susceptible factors, H. pylori, and other gut microbes influence the host molecular and cellular activities, leading to the development of gastric cancer. Our study will identify candidate synergistic factors with H. pylori in gastric carcinogenesis, with ex vivo verification using organoid models.

Objectives: We have three aims. First, we will define host genomes transcriptomes and gut microbiome profiles in H. pylori positive and negative gastric cancer patients respectively. We will include four groups of human patients based on the diagnosis of gastric cancer (with/without) and presence of H. pylori (+/-). Microbiota profiles, genomic and transcriptomic profiles will be profiled and collected for each patient sample. Second, we will identify the influences of gut microbes (including H. pylori) and host genetic susceptible factors on gastric

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carcinogenesis through integrative analysis. Ontology-based computational and statistical methods will be developed to help integrate and analyze multi-layered datasets. Bayesian network method will be applied to evaluate and predict relations among multiple factors. Third, we will verify hypotheses generated in Aim 2 on the contingent influence of H. pylori and host-microbiota interactions, using in-house developed patient-derived gastric organoid models. The verified hypotheses could be validated in the future in collaboration with gastric epidemiologists at the hospital.

Expected Outcomes: This systematic study will identify candidate synergistic factors with H. pylori in gastric carcinogenesis and provide proof-of-concept ex vivo experimental verification using organoid models, leading to further understanding of gastric carcinogenesis.

Inflammatory Mediators of Cardiac and Other End Organ Dysfunction During Venoarterial Extra-corporeal Membrane Oxygenation

Co-Investigators

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Cardiovascular disease is the leading cause of death in the world. The use of extracorporeal membrane oxygenation (ECMO) for the treatment of cardiopulmonary collapse has risen exponentially. Data from the Extracorporeal Life Support Organization (ELSO) show that 86,287 cases of extracorporeal membrane oxygenation were performed in 2017. Of these 10,982 cases were performed for cardiogenic shock. Thus the complications and morbidities of ECMO has an enormous impact on resource utilization as well as patient outcomes. A major complication that impairs patient survival is the impairment of end organ function associated with ECMO induced inflammation. Furthermore this inflammation can impact myocardial recovery and predict right heart failure after bridge of ECMO to a left ventricular assist device (LVAD). Right ventricular failure after LVAD implant is also a predictor of prolonged hospitalization as well as increased patient morbidity and mortality. Our objective is to determine the association of ECMO mediated inflammation with end organ dysfunction including impairment of myocardial function. Distinct from previous studies, this investigation will focus on patients undergoing venoarterial ECMO for cardiogenic shock either in the setting of acute cardiac decompensation or failure to wean from cardiopulmonary bypass after cardiac surgery. By collecting serum samples and determining leukocyte activation, we will correlate inflammatory markers as well as leukocyte activation with clinical outcomes of ECMO. The outcomes studied include end organ dysfunction (e.g. renal, pulmonary,

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brain), myocardial recovery, right heart failure after bridge to LVAD, and mortality on ECMO. Furthermore, we will perform mechanistic in-vitro studies in patients who are bridged to LVAD where we can obtain leukocytes and myocardium from the same patient. Using an in-vitro leukocyte and myocardium co-culture model, we will determine human myocardial responses to leukocyte activation.

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Delegation from China: Biographies for the visiting delegation members from PKUHSC

BAI, Jing 白婧
CHEN, Xiuyuan 陈修远
CHEN, Yahong 陈亚红
CONG, Yali 丛亚丽
DONG, Erdan 董尔丹
DUAN, Liping 段丽萍
FANG, Weigang 方伟岗
FANG, Zhengyu 方征宇
GE, Xiyuan 葛兮源
GONG, Kan 龚侃
GU, Yan 谷岩
GUO, Chuanbin 郭传瑸
HAN, Jiangli 韩江莉
HE, Bei 贺蓓
HONG, Baoan 洪保安
HU, Xiaoqing 胡晓青
HUANG, Rui 黄睿
HUANG, Yining 黄一宁
JIANG, Yanfang 蒋艳芳
KONG, Yan 孔燕
LI, Huijuan 李会娟
LI, Jianping 李建平
LI, Ming 李明
LI, Nan 李楠
LI, Qing 李箐
LI, Shuo 李硕
LI, Xiaojia 李晓佳
LI, Zhao 李照
LI, Ziyu 李子禹
LIU, Hong 刘虹
LIU, Jixian 刘继先
LIU, Ran 刘冉
LIU, YaJie 刘源
LIU, Yuan 刘源
LU, Lin 陆林
LUO, Dasheng 骆大圣
MA, Qingbian 马青变
MENG, Shiqiu 孟适秋
MU, Rong 穆荣
PAN, Kaifeng 潘凯枫
PENG, Yun 彭芸
QI, Huiying 齐惠颖
RAO, Huiying 饶慧瑛
SHEN, Ning 沈宁
SHI, Jie 时杰
SHI, Yu 石宇
SONG, Yuqin 宋玉琴
SU, Jiazeng 苏家增
SUN, Qiudan 孙秋丹
WAN, Feng 万峰
WANG, Deli 王德利
WANG, Fangfang 王芳芳
WANG, Guisong 王贵松
WANG, Jianliu 王建六
WANG, Jingmin 王静敏
WANG, Tao 王涛
WANG, Weimin 王维民
WANG, Xiaoyan 王晓燕
WANG, Yanfang 王燕芳
WEI, Lai 魏来
WU, Jianmin 吴健民
WU, Jing 武靖
WU, Ping 吴萍
WU, Song 吴松
WU, Yangfeng 武阳丰
XIAO, Han 肖晗
XIAO, Yu 肖瑜
XIE, Ana 谢阿娜
XIE, Bing 谢冰
XIE, Gaoqiang 谢高强
XIE, Guangkuan 谢广宽
YAN, Liying 闫丽盈
YANG, Ence 杨恩策
YANG, Fan 杨帆
YANG, Hongyu 杨宏宇
YANG, Ming 杨明
ZHAN, Qimin 詹启敏
ZHANG, Hongyu 张红宇
ZHANG, Lianhai 张连海
ZHANG, Nannan 张楠楠
ZHANG, Ning 张宁
ZHANG, Wei 张薇
ZHANG, Xiaotian 张小田
ZHANG, Xuehui 张学慧
ZHANG, Yan 张岩
ZHANG, Youyi 张幼怡
ZHANG, Zhe 张喆
ZHENG, Shuguo 郑树国
ZHENG, Ya'an 郑亚安
ZHOU, Jing 周靖
ZHOU, Jingcheng 周靖程
ZHU, Shiwei 朱诗玮
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Jing Bai received her BA in Biomedical English in 2013 from PKU before enrolling in a three-year master's program in the School of Public Health. During the program, she focused on global health, especially the product research and development for neglected diseases. Jing was a research assistant in the Department of Global Health, School of Public Health at PKU, and participated in several research programs including China's Health Research and Development and Public Health Equity, Policy and Implementation Experience of Child Nutrition in China, and China's Distinctive Engagement in Global Health. In addition, she was an event coordinator in the department and organized or assisted in dozens of meetings or trainings, such as PKU-DUKE Global Health Certificate Program, Chinese HIV/AIDS-related Post-MDG Consultation Seminar, Duke Global Semester Abroad Program, and more.

After she obtained her MSc, she began to work in the Office of International Cooperation, Peking University Health Science Center in August, 2016. She is currently responsible for developing partnerships with overseas universities, scientific research institutions, NGOs, and companies.

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Dr. Chen is a thoracic resident of the Department of Thoracic Surgery at Peking University People's Hospital. After his MD training in Peking University, he pursued thoracic surgery residency at Peking University People's Hospital along with a post-doctoral research fellowship at the University of Michigan. He has a background and training in thoracic surgery, molecular biology and artificial intelligence. His clinical interests include fluorescent aided minimally invasive thoracic surgery, AI-assisted lung cancer diagnosis, and multi-disciplinary treatment for advanced lung cancer. His research focus includes circular RNA in lung cancer, autophagy and immune-therapy. He is an International Member of the Society of Thoracic Surgeons.

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Dr. Chen earned her MD degree at Southeastern University in 1994 and her PhD degree at Peking University in 2001. She was a visiting scholar at the University of Michigan in 2010-2011. Her research interests are translational clinical research in chronic inflammatory airway diseases including COPD and asthma. She has participated in the China Pulmonary Health (CPH) study (published in *The Lancet* in 2018), investigating the incidence of COPD in China and the risk factors. Dr. Chen's joint project with Dr. Steve Huang at UM and Professor Furong Deng at the PKU School of Public Health explores the effect of air pollution on DNA methylation in patients with uncontrolled asthma in China. She has been supported by the National Natural Science Foundation of China for research on the mechanism of gasotransmitter hydrogen sulfide in the airway inflammation and airway remodeling in COPD and asthma and has published peer-reviewed papers.

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Yali Cong is a Professor in Bioethics, Dean of the Department of Medical Ethics and Health Law, and Chair of Peking University Institutional Review Board (PKU IRB). Prof. Cong earned her PhD in Philosophy and has a wide range of research interests, including Research Ethics, Public Health Ethics and Medical Professionalism. She has published a variety of papers in the field of Bioethics and research teams on projects from the China Philosophy and Social Science, the Wellcome Trust, the Fogarty of National Institute of Health, etc. Prof. Cong took her position as PU IRB Chair in June 2010 and has been devoted to institutional capacity building and policy-making in regards to human subject protection at Peking University. She is team-leader of the working group that helps the Peking University Human Research Protection Program (PKU HRPP). She was recently designated the Chair of China Medical Ethics Association.

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Dr. Dong received his MD from Peking University and continued his postdoctoral work at University of Rochester. He was a professor at Peking University Third Hospital from 2000 to 2008, and was Executive Deputy Director of the Department of Health Sciences of the National Natural Science Foundation of China (NSFC) from 2009 to 2017. His research interests are in vascular medicine and healthcare technology engineering. Dr. Dong hosted and participated in several research projects of the NSFC and National Science and Technology Academic Works Publication Fund, and has published over 130 papers. He serves as associate editor for several journals including Science China Life Sciences, Chinese Medical Journal, Chinese Journal of Cardiology, and Chinese Journal of Hypertension. He is the member of Huaxia Medical Science and Technology Award Council, the member of China Association for Science and Technology (CAST) academic board, the Chair of Chinese Society for Vascular Medicine. He obtained Ho Leung Ho Lee Foundation the Science and Technology Innovation Award in 2014; China Medical Research Management Outstanding Contribution Award in 2017; and has obtained special government allowance from the State Council since 2013.

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Dr. Duan received her MB in 1986 at the Department of Clinical Sciences of the Beijing Medical University followed by her MD in 1991. From 1992 to 1995, she was the postdoctoral fellow at the Division of Gastroenterology of Goethe University, Germany. She was the senior visiting scholar at the Division of Gastroenterology at Beth Israel Deaconess Medical Center (BIDMC) of Harvard Medical School from 2001 to 2002. Now, she is the Member of the Disciplinary Assessment Panel of the Academic Degree Committee of the State Council; a member of the Academic Degree Committee of Beijing; Standing Director of the Chinese Society of Academic degrees and Graduate Education (CSADGE); Deputy Chief and Secretary General of the Medical and Pharmaceutical Division of the CSADGE; Secretary General of the National Steering Committee on Medical Degree Education; and a committee member of the Chinese Society of Gastroenterology. Dr. Duan's core interest is in neurogastroenterology and motility. Her current research is investigating the comorbidity of psychiatric disorders and chronic gastrointestinal diseases, as well as the interaction of intestinal flora and brain-gut axis function. She has more than 100 publications in both international and Chinese journals.

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Prof. Fang received his PhD (1991) at the Dept of Pathology, Beijing Medical University. As the Associate Director of Peking University Cancer Research Center and head of Molecular Pathology, his research interest has focused on molecular mechanisms of cancer metastasis. In his academic career Prof. Fang has been a PI on more than 30 peer-reviewed research projects and has published more than 120 research papers. He served as Vice President of PKUHSC for Research and International Cooperation for 10 years, and currently is Director of the Peking University Clinical Research Institute.

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Dr. Fang received his MD from Shanghai Medical College of Fudan University in 2003 and a PhD from the same school in 2008. He has been working in Shenzhen-PKU-HKUST Medical Center as a post-doc and then an assistant professor. He has long been engaged in the research of tumor biology, including the relationship between integrin abnormalities and the development of malignant tumors. After cooperating with the clinical department of Peking University Shenzhen Hospital, Dr. Fang carried out a series of research on cancer-related long non-coding RNA, mechanisms of tumor resistance and sensitization. In the field of tumor resistance research, a number of drug-resistant strains of different tissue-derived tumors were constructed, and a series of non-coding RNAs related to drug resistance were screened and intensively studied. As a project leader, he has obtained a number of scientific research projects at the national, provincial and municipal levels. He has published more than 30 scientific papers on Journals like Journal of Cell Biochemistry, BMC Cancer, and Oncotarget, etc.

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Dr. Ge's research interests are oral and maxillofacial tumors as well as salivary gland diseases. He has published scientific articles in *Theranostics*, *Oncotarget*, *Anticancer Drugs*, and *Oral Oncology*, to name a few.

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Dr. Gong's research focuses on urological oncology, especially renal cell carcinoma. Since 1998, his team has been conducting systematic research on the genes relative to renal cancers, especially von Hippel-Lindau (VHL) gene and its downstream molecules under the support of successive national funds (over $ 1,000,000). He also summarized the characteristics of Chinese patients with VHL disease (the most common hereditary renal cancer), and revealed the mechanism of the VHL gene. He has a patent for diagnosing VHL patients through a genetic test and has promoted this method to other hospitals in China. Also, he is the only member of the advisory committee of the VHL Family Alliance International in China. Dr. Gong's team has established a biobank of renal cancers which include more than 200 specimens of sporadic or VHL disease associated renal cell carcinoma. Now they are working hard to study the possible mechanism of renal cell carcinoma and VHL disease. He has been awarded many national research grants and received the highest state-level scientific research award in China, the third prize of the Chinese Medical Scientific Award.

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Professor Yan GU received dental degree and orthodontic training from Beijing Medical University (predecessor of Peking University Health Science Center) and a PhD in Orthodontics from the Faculty of Dentistry, The University of Hong Kong. She visited the U-M School of Dentistry's Department of Orthodontics and Pediatric Dentistry from 2005-2006 and collaborated with Professor James A. McNamara on research on craniofacial growth.

Her major research interest includes craniofacial growth and development and regeneration of periodontium defects, with a particular focus on proteomic analysis of gingival crevicular fluid for novel biomarkers to indicate pubertal growth peak. She is also working on multiple clinical projects in the area of orthodontic esthetics and the stability of treatment effects of skeletal Class III malocclusion. In 2009, she received the Edward H. Angle Research Prize for a study on mandibular growth changes related to Cervical Vertebral Maturation Method.

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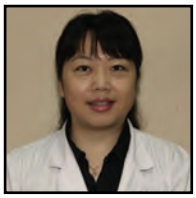
Professor Guo graduated in 1985 from School of Stomatology, Shanghai Second Medical University and obtained a PhD at Beijing Medical University School of Stomatology in 1992. In addition to his role as Dean of the School and Hospital of Stomatology Peking University, Guo also serves as Vice President of the Chinese Stomatological Association; Vice Director of Head and Neck Surgery Committee of China Anti-cancer Association; and is one of the Board Directors of ADT (Advanced Digital Foundation) Foundation. He is a member of the editorial board for eight medical journals.

Professor Guo is engaged in clinical and laboratory study on oral and maxillofacial surgery and is highly experienced in the diagnosis and treatment of oral tumors, as well as tumors in parapharyngeal space and infratemporal fossa and tumors involving the skull base. His innovations include using sternocleidomastoid muscle-great auricular nerve flap to reconstruct the accessory nerve defects; designing a new surgical approach for handling tumors in the skull base; and developing an automatic robot to assist mandible reconstruction. His current research interests focus on Bifidobacterium Adolescentis as a delivery system for gene therapy of oral cancers, and digital technique application in the management of head and neck surgery. The author of 176 scientic papers, Guo has recieved numerous awards for achievements in scientific and clinical studies.



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Dr. Han is Chief Physician and Associate Professor of Cardiovascular Medicine at Peking University Third Hospital and also the director of the Education Department. She obtained her MD and PhD from Peking University Medical School before joining the cardiovascular department in Peking University Third Hospital. She studied as a fellow at the Texas Heart Institution at St. Luke's Episcopal Hospital from November 2010 to October 2011. In 2014, Dr. Han was promoted to Chief Physician. Currently, she is a member of the National Health Talent Evaluation Center of the Ministry of Health Talents, a member of the Women's Medical Group of the Chinese Medical Association Cardiovascular Disease Branch, and a reviewer of *Peking University Journal* (Medical Edition).

An experienced clinician and researcher, Dr. Han specializes in percutaneous coronary intervention (PCI) and has performed over 3000 cases of emergency and elective PCI procedures. As for clinical research, she has participated in many research projects such as China Coronary Study of Diagnosis (CCSD) supported by the National Institute of Science in China. In addition to clinical work and research, she has also been devoted to student teaching. She was awarded the Excellent Teaching Award by Peking University in 2013 and the Outstanding Head Teacher one year after. As Director of the Education Department of the Peking University Third Hospital, she is responsible for the teaching management of medical student education, post-graduate education and continuing medical education.

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As a Chief Physician in the Radiology Department of PKU Third Hospital, Dr. Han is in charge of both the office of Scientific Research and the office of Discipline Construction, Peking University Health Science Center.

Dr. Han established the Beijing Key Laboratory of Magnetic Resonance Imaging (MRI) Equipment and Technique and has served as the center's Director since 2010. He has authored 5 monographs, has published more than 200 research articles, and garnered 15 patents. His research group focuses on advanced MRI techniques for diagnosis and therapy of brain diseases, especially developing novel techniques of in vivo extracellular space (ECS) imaging. The method he invented has led to the discovery of a glymphatic drainage route in deep brain, which inspired the regional brain homeostasis theory. His team further developed a new drug delivery method, Simple Diffusion Delivery (SDD). These cutting-edge technical inventions and scientific discoveries broaden the knowledge of neuroscience, highlight deep learning in artificial intelligence and brain tissue engineering fields, and provide new prospective to many fields including life science, clinical medicine, drug discovery, and traditional Chinese medicine.

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Dr. He's primary research areas include lung infections and chronic obstructive diseases with six National Natural Science Foundation of China (NNSFC) grants and nine other grants (from Ministry of Education Doctoral Program, Ministry of Health, Beijing Natural Science Foundation, Capital Development Funds), 3 international grants (NIH grant and JI grants as CoPI), and more than 150 publications (including publications in Chinese and English). Her JI work explores biomarkers, microbiomics and metabonomics in the pathogenesis of COPD with UM experts. In the area of lung infections, she finished CAP and HAP studies, and population pharmacokinetic (PPK) researches of meropenem, vancomycin and ciprofloxacin. She also joined in national epidemiological survey of pathogenic bacteria and new national guidelines formulation in CAP and HAP. She has been working on several clinical trials of drugs as PI and Co-PI. Dr. He is a member of the standing committee of the Respiratory Branch of Chinese Medical Association; Vice Chairman, Infection Disease Division, Respiratory Branch, Chinese Medical Association; Vice Chairman of Respiratory Branch, Chinese Medical Women's Association; member of the Chinese Medical Doctor Association Standing committee; Global Governor of College of Chest Physicians Global Council, FCCP; and a member of ATS, ERS and APSR.

Baoan Hong, MD
Department of Urology
Peking University First Hospital

Email: 1074578543@qq.com

Dr. Hong earned his MD from Capital Medical University in 2013 and is currently a PhD candidate and research fellow in Urology at PKU First Hospital, studying under Professor Kan Gong. The primary focus of his research is the mechanism of renal cell carcinoma.

Xiaoqing Hu, PhD
Associate Professor of Sports Medicine
Institute of Sports Medicine
Peking University Third Hospital

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Dr. Hu graduated from Peking University with a PhD degree in Biochemistry and Molecular Biology in 2010. Then she worked for two years as the postdoctoral fellow at Institute of Sports Medicine, Peking University Third Hospital. Her main research interests include: (1) regeneration of articular cartilage; (2) stem cell biology, biomaterials and tissue engineering; and (3) epigenetic regulation of stem cells in osteogenic process. She is responsible for project coordination while developing her own research interest on clinical trials. She has experience in clinical medicine, basic research, and translational research and has published papers about chondrogenesis of stem cells and their epigenetic regulation. She has also successfully applied for the grants of China Postdoctoral Science Foundation and the National Natural Science Foundation of China as PI.

Yining Huang, MD, PhD
Chairman and Professor
Department of Neurology
Peking University First Hospital

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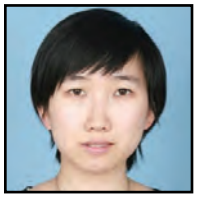
Professor Huang received his doctoral degree from Peking Union Medical College and has dedicated himself to his clinical practice. He has served as principal investigator on a number of clinical trials focusing on stroke. He has received grants for leading several national projects and Chinese scientific committee grants for his work establishing guidelines for clinical diagnosis and management of acute stroke in China, as well as the establishment of a national platform for new drug evaluation on stroke.



Rui Huang, MD
Peking University Hepatology Institute
Peking University Second Hospital

Email: strangehead@163.com

Dr. Huang graduated from Peking University Medicine Science Center with an MD in internal medicine before going to work in the hepatology department of Peking University People's Hospital as an attending physician in hepatology in 2015. She has been engaged in the diagnosis and treatment of non-alcoholic fatty liver disease, viral hepatitis, and complications of cirrhosis in the outpatient and inpatient departments. Dr. Huanzg has participated in three clinical trials of viral hepatitis and four clinical research projects of viral hepatitis and non-alcoholic fatty liver disease. She has published three papers on viral hepatitis C and non-alcoholic fatty liver disease and presented posters at the 2016 CSH-AASLD joint forum; 2017 APASL; and 2018 AASLD. She garnered an excellence award in Liver Disease Clinical Thinking Training Camp in 2016 and the first prize paper award in the 8th National Academic Conference on Non-alcoholic Fatty Liver Disease and Alcoholic Liver Disease in 2018. In addition, she was hired as a youth editor of *GUT* (Chinese edition) in 2018.

PKUHSC Delegation

北京大学医学部代表团成员名单

Yanfang Jiang, MSc
Research Technician
Institute of Sports Medicine
Peking University Third Hospital

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Yanfang Jiang graduated from Peking University with honors in 2009 with a bachelor's degree in Biomedicine and English and a double degree in Psychology before pursuing her master's degree in Epidemiology from London School of Hygiene and Tropical Medicine in 2014. Currently, her main research interest is outcomes evaluation of the surgical and conservative management of sports injuries, aiming to provide evidence to the optimum clinical care and individualized care. She has been working on developing an electronic data capture system to integrate routine clinical data, research project-derived data, and internet-based follow-up questionnaires, and has obtained skills in database development as well as patient recruitment/ tracking in clinical trials and cohorts. She is also working on the translation and validation of patient-reported outcome measures (PROs) for use in the Chinese language.

Yan Kong, PhD
Associate Professor
Department of Renal Cancer & Melanoma
Peking University Cancer Hospital

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Yan Kong majored in clinical medicine and graduated from Harbin Medical University in 2001, and then obtained a master's degree in biochemistry and molecular biology from Peking Union Medical College in 2005 and a PhD in immunology from Peking Union Medical College in 2008. She began her career in the Department of Renal Cancer and Melanoma at Peking University Cancer Hospital in 2008 and has been responsible for melanoma and renal cancer molecular biomarker research design, implementation and supervision. As a core member of the team, she explores individualized targeted therapy for melanoma and renal cancer, and has made essential achievements in melanoma gene mutation and individualized molecular targeted therapy in particular, which has been promoted nationwide. Dr. Kong has carried out two projects funded by the National Natural Science Foundation and three projects of provincial level. She has published more than 30 peer-reviewed articles on domestic and international journals. One of her articles has been cited 342 times.

Huijuan Li, PhD
Deputy Director & Research Fellow
Department of Project Development and Management
PKU Clinical Research Institute

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Dr. Li earned her bachelor's in preventive medicine from Peking University in 2004 and her PhD in 2009 at Peking University Third Hospital's Research Center of Clinical Epidemiology. She was a visiting scholar at Duke University in 2012 and is currently a Research Fellow at the Peking University Clinical Research Institute where she provides guidance to investigators on issues like inclusion/exclusion criteria, treatment measurement, sample-size evaluation, safety concerns, etc. She also helps departments prepare proposals for IRB submission and develops procedures and best practices for project management and monitoring.

北京大学医学部代表团成员名单

PUKHSC Delegation

Jianping Li, MD, PhD
Professor, Executive Deputy Director
Department of Cardiology
Peking University First Hospital

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Dr. Jianping Li graduated from Peking University Health Science Center in 1992 and received his PhD in Peking University First Hospital, Department of Cardiology, in 1998. He received training on Population Genetics at the Harvard School of Public Health (1999 to 2003) before returning to PKU First Hospital. He is now the Vice President of Coronary Intervention Committee, Chinese College of Interventional Physicians (CCI); and Vice President of Branch of Prevention and Treatment of Cardiovascular Disease, China International Exchange and Promotion Association for Medical and Healthcare. His research interests have been focused on 'H type' hypertension (hypertension accompanied with high homocysteine level) and folic supplementation in stroke prevention in China.

Dr. Li found that high homocysteine level significantly amplified the risk of stroke in Chinese hypertensives, whereas folic acid supplementation significantly reduced the risk of stroke on the basis of blood pressure control, work that was published in JAMA in 2015. More than 30 manuscripts had been published in this research filed, and he was awarded as the second prize of National Science and Technology Advancement Award (2nd investigator) in the year 2016. In his latest JI project, Dr. Li will collaborate with Professors Daniel Eitzman and Haoming Zhang to investigate using a new antiplatelet agent to overcome the inter-individual variability of antiplatelet therapy.

Ming Li, MD
Associate Professor
Child Development and
Neuro-habilitation Clinic
Department of Pediatrics
Peking University First Hospital

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As a senior pediatric neurologist in a leading hospital in China, Dr. Li has expertise in the diagnosis and management of a variety of developmental disorders. In 2001, he set up a child neuro-habilitation clinic in PKUHSC First Hospital. His research focuses on child neurodevelopmental and behavioral assessments and their interpretation, covering both motor and mental development, from newborns to adolescents, and includes national and international collaborations. As PI, his research projects have looked at the relation between gene mutations and autism in males and assessed motor development in relation to cerebral palsy in high-risk infants. As co-investigator, he has collaborated with a team from Sweden to develop, set up, and implement a training model for screening for mental retardation in young children (0-6) across five counties. For the past 10 years, he has been working with Dr. Betsy Lozoff (UM) on an NIH-supported, large-scale, iron study in rural China, training local staff to understand and administer assessments for all ages. In the environmental exposures study, he is responsible for the day-to-day logistics of specimen collection and transport. In a proposed epigenetics pilot study, he will also assist in analysis and interpretation of neurodevelopmental outcomes as they relate to environmental exposures, iron status, and epigenetic changes.

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北京大学医学部代表团成员名单

Nan Li, PhD
Associate Professor of
Clinical Epidemiology
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Professor Li is the Secretary and a member of Methodological Group of the Beijing Society of Clinical Epidemiology and Evidence-Based Medicine (a Beijing Medical Association Specialty Societies), as well as a committee member of the Medicine Economics Professional Committee, China Research Hospital Association. His primary research interests are clinical epidemiology, clinical research methodology and biostatistics. Professor Li leads a project, Estimation and Correction Method of Missing Diagnosis in Dementia Prevalence Survey Based on Missing Data Processing Model and LRS Theory, which is supported by the National Natural Science Foundation for Young Scholar Fund. He participated in another project, Constriction demonstration of collaborative network construction of clinical research, funded by the Ministry of Science and Technology, to build up the common technology service platform of a national clinical research center and support collaborative network construction. He has provided clinical research expertise and training services for many academic institutions and international pharmaceutical companies and has published more than 50 articles, including 15 first-author/co-author papers.

Qing Li, DMD, PhD
Lecturer, Center of Digital Dentistry,
Peking University School and Hospital of Stomatology
National Engineering Laboratory for Digital and Material Technology of Stomatology

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Dr. Li graduated in 2006 from West China College of Stomatology, Sichuan University, with a doctoral degree in dentistry. After graduation, she went to the Ninth People's Hospital affiliated with Shanghai Jiao Tong University as faculty. In 2009 Dr. Li, came to Peking University School and Hospital of Stomatology and in 2015 completed her postdoc working in biomedical engineering at the Beihang University. In 2017, Dr. Li came to the U-M School of Dentistry to work as the visiting scholar in the Department of Periodontics and Oral Medicine. Her research areas include cells bioprinting technology, including accurately deposit different kinds of cells in specific time and space; 3D printing of alveolar bone, periodontal ligaments, salivary glands and trigeminal nerve; and maxillofacial soft and hard tissue regeneration. She has published 6 SCI articles and 4 invention patents.

Shuo Li, MD
Associate Chief Physician
Department of Emergency Medicine
Peking University Third Hospital

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Shuo Li received her bachelor's degree in clinical medicine from Norman Bethune University Medical School in 2000 and her master's in Neurology from Jilin University First Hospital in 2003 before going to work in the Emergency Department of Peking University Third hospital. She has been an Associate Chief Physician since 2015. She spent three months as a visiting scholar at the UMMS Department of Emergency Medicine in 2017. Her past training and research work focused on neurological diseases/emergency/COPD. At the PKU Third Hospital Emergency Department, she has been mainly in charge of the resuscitation room and EICU. She is proficient at using techniques such as cardiopulmonary resuscitation, endotracheal intubation, central venous catheter, PICCO, and CRRT in critically ill patients. Most recently, she is focused on therapeutic hypothermia for cardiac patients after resuscitation and ECPR.

北京大学医学部代表团成员名单

PUKHSC Delegation

Xiaojia Li, MSc
Chief, Division of Exchange
Office of International Cooperation
PKUHSC

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Xiaojia LI, MSc, is the Chief of the Division of Exchange of Office of International Cooperation, Peking University Health Science Center (PKUHSC). She has been working in the Office of International Cooperation since 2005. She is responsible for developing partnerships with overseas universities, scientific research institutions, NGOs and companies, receiving visits from international professors, experts, and faculty, and managing overseas exchange programs.

Zhao Li, MD, PhD
Associate Professor of Surgery
Department of Hepatobiliary Surgery
Peking University Second Hospital

Email: lizhao@bjmu.edu.cn

Dr. Li's specialty is liver transplantation, liver cancer and portal hypertension. He has finished more than 100 cases of donor liver procurements and is very experienced in treating end-stage liver diseases. He engaged in advanced training of liver transplantation at Cleveland Clinic in 2010 and also spent one year at UMMS in 2015 to learn molecular imaging techniques. Meanwhile, he participated in plenty of basic research programs about liver cancer and liver transplantation and published several papers in the field. In 2016, he garnered a grant from the Natural Science Foundation of China for HCC research: Modeling the defined microenvironment of intrahepatic metastasis from hepatocellular carcinoma through muti-cellular co-culture in decellularized scaffold. He had explored several HCC biomarkers based on huge HCC bio-bank samples, especially of GPC-3, and found close correlation between GPC-3 expression level and patient prognosis.

Ziyu Li, MD
Professor & Chief of Gastrointestinal
Surgery Center Ward I
Vice Chief of Surgery
Peking University Cancer Hospital

Email: ligregory@outlook.com

Dr. Li earned his MD in 1995 from Qingdao Medical College and his PhD in 2002 from Tongji Medical College, Hauzhong Science and Technology University. He joined the Peking University Cancer Hospital in 2005 and was an international fellow in colorectal surger at the University of Sydney-affiliated Concord Hospital from 2009-11. His research has appeared in *Gastric Cancer*, *PLoS One*, the *Journal of Pathology*, and more.

PKUHSC Delegation

北京大学医学部代表团成员名单

Hong Liu, MD
Associate Director
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Peking University Health Science Center

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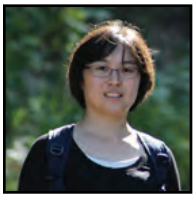
Hong Liu works in the Department of Education, Peking University. As an Associate Director, Dr. Liu is in charge of the teaching affairs of medical education. She graduated from Beijing Medical University and received clinical training in Pediatrics at Peking University Third Hospital. Since 2005, Dr. Liu's main interest has been in medical education. She has taken part in the work of online education, teaching development and domestic collaboration.



Ran Liu, MD
Associate Chief Physician
Department of Neurology
Peking University First Hospital

Email: dyyxys@126.com

Dr. Liu received her doctoral degree from Peking University Health Science Center and has dedicated herself to clinical practice as well as serving as an investigator on a number of clinical trials focusing on stroke. She also received grants from Chinese scientific committees and applied herself to the pathophysiological mechanisms in ischemic stroke.

YaJie Liu MD, PhD
Chief Physician
Director, Department of Radiation Oncology
Peking University Shenzhen Hospital

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Dr. Liu earned her degree in clinical medicine at Buthane Medical University in 1990 and her master's and doctorate in radiation oncology at Harbin Medical University and Peking Union Medical College, respectively. She has been with Peking University Shenzhen Hospital since 2017. Prior research areas have included: hyper-fractionated radiotherapy in nasopharyngeal carcinoma and chemotherapy sensitizer for radiotherapy; radiation encephalopathy after radiotherapy for head and neck carcinoma; radiosensitization of arsenic trioxide in nasopharyngeal carcinoma and its mechanism; 3D-CRT vs VMAT in Combination with Xelox (capecitabine plus oxapfiplatin) preoperative neoadjuvant chemoradiotherapy for locally advanced rectal cancer; and prediction of local recurrence risk of early breast cancer with 21gene. A new research interest is investigating radiosensitive biomarkers and molecular-targeted therapies combined with radiotherapy.

北京大学医学部代表团成员名单

PUKHSC Delegation

Yuan Liu, MBA
Program Officer
Office of International Cooperation
Peking University Health Science Center

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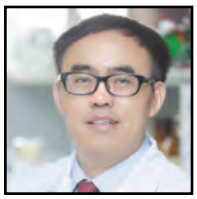
Yuan Liu graduated in 2011 with a bachelor's degree in English from Shanxi Normal University. In 2013, he graduated from China Foreign Affairs University with a second bachelor's in Diplomacy before joining the Office of International Cooperation in the summer of 2013. Mr. Liu received a master's in Public Administration from China Foreign Affairs University in 2013. He is currently responsible for developing partnerships with overseas universities, scientific research institutions, NGOs, and companies, with a particular focus on partnerships in the Americas.

Jixian Liu, MD
Chief Physician
Deputy Director of Thoracic Surgery
Peking University Shenzhen Hospital

Dr. Liu was recently named Chief Physician in the Department of Thoracic Surgery, Peking University Shenzhen Hospital. His clinical and research interests have centered on the diagnosis and treatment of thoracic disease, especially through minimally invasive methods. Specifically, his focus is on the anti-apoptosis gene, bcl- 2, especially in lung cancer.



Lin Lu, MD, PhD
Director/Professor
Institute of Mental Health
Peking University Sixth Hospital
Director of the National Institute
on Drug Dependence, PKUHSC

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A member of the Chinese Academy of Sciences, Dr. Lu is Director of National Clinical Research Center for Mental Disorders and the National Center for Mental Health of Chinese Center for Disease Control and Prevention. He is also a principal investigator of PKU-IDG/McGovern Institute for Brain Research and Peking-Tsinghua Center for Life Sciences. Dr. Lu is an associate editor of *Drug and Alcohol Dependence* and the *American Journal on Addictions*; an editor of *Sleep Medicine Reviews* and the *International Journal of Neuropsychopharmacology and Addiction*; and an editorial board member of both the *International Journal of Mental Health and Addiction* and the *American Journal of Drug and Alcohol Abuse*. He has been a reviewer for over 40 international journals, including *Nature*, *Science*, *Nature Medicine*, and *Nature Neuroscience*.

Dr. Lu's research focuses on the neurobiological mechanisms and clinical intervention measures of psychiatric disorders (e.g. substance addiction, sleep disorders and depression), including aberrant synaptic plasticity of depression and drug dependence, the molecular mechanisms of dynamic pathological memory, and psychological and cognitive changes in depressive patients, drug addicts and patients with sleep disorders. Using comprehensive behavioral, molecular, pharmacological, psychological and neuroimaging techniques, Lu's lab has made substantial progress that contributes to the understanding of the pathogenesis of psychiatric disorders. Dr. Lu has published over 200 high-level research articles in leading journals in the fields of psychiatry and neuroscience, including *Science*, *JAMA Psychiatry*, *American Journal of Psychiatry*, *Biological Psychiatry*, and *Molecular Psychiatry*.

PKUHSC Delegation

北京大学医学部代表团成员名单

Dasheng Luo, MPH
Office of International Affairs
Peking University Cancer Hospital

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Mr. Luo obtained a master's degree in health policy and management with concentration on global health from Peking University Health Science Center in 2013, and has been working in the Office of International Affairs of Peking University Cancer Hospital ever since. His responsibilities are mainly expanding and deepening the hospital's relations with international counterparts; coordinating and organizing international academic exchange activities; and facilitating and monitoring implementation of international cooperation programs.

Qingbian Ma, MD
Emergency Department Vice Chair
Peking University Third Hospital

A graduate of Peking University, Dr. Ma is an Associate Professor of Emergency Medicine and the Vice Chair of the Emergency Department in PKUHSC Third Hospital. She is also a member of the Chinese Clinical Emergency Physicians; a member of the Chinese Society for Emergency Medicine; Vice Chair of Beijing Medical Association for Emergency Medicine Youth committee; and an instructor of the American Heart Association's cardiovascular ACLS training program. She has abundant clinical experience in emergency and critical care and is interested in clinical research on cardiovascular emergencies and hypothermia after cardiac arrest. She has a keen interest in medical training, especially in medical simulation training.

Shiqiu Meng, PhD
National Institute on Drug Dependence
Peking University

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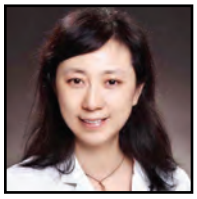
Professor Shiqiu Meng obtained her bachelor's of medicine from the Ocean University of China (majoring in Pharmacy) in 2011; an MSc from the University of Edinburgh, UK, in Drug Discovery and Translation Biology in 2012; and her PhD in Pharmacology from Peking University in 2016. She is engaged in research on the neurological mechanisms and interventions of drug addiction, aging-related cognitive impairment, and depression, and has completed several research projects about social facilitation of drug relapse, epigenetic mechanisms underlying aging-related cognitive impairment, as well as antidepressant-like effects of novel MBP-altered peptides. Professor Meng has published 18 papers in SCI journals and obtained an authorized patent on preparation of antidepressants. She is also a reviewer for *Drug and Alcohol Dependence*.

北京大学医学部代表团成员名单

PUKHSC Delegation



Rong Mu, MD
Professor of Rheumatology
Director, Department of the International Affairs Office
Peking University Second Hospital

Email: murong@pkuph.edu.cn

Dr. Mu is a Professor of Rheumatology in Peking University People's Hospital. She is a clinical physician with particular interests in rheumatic diseases. Her research interests include understanding the pathogenesis of autoimmune inflammatory diseases, both from the basic laboratory perspective of proinflammatory molecules and cells and using a translational medicine approach for therapeutic utility. This year, she has published articles in *Pharmacogenomics*, *Chinese Medical Journal*, and the *The International Journal of Rheumatic Diseases*.

Kaifeng Pan, MD, PhD
Professor of Epidemiology
Director, Department of Cancer Epidemiology
Vice President, Peking University Cancer Hospital & Institute

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Dr. Pan is a professor of epidemiology, Director of Department of Cancer Epidemiology, Vice President of the Peking University Cancer Hospital & Institute, Deputy Director of the Key Laboratory of Carcinogenesis and Translation Research (Ministry of Education), and Director of the Sino-German Joint Key Laboratory. Dr. Pan is a member of the International Gastric Cancer Association (IGCA), the Co-Chairman of China Anti-Cancer Epidemiology Association, and the Chairman of China Anti-Cancer Epidemiology Association Youth Committee. She received her Master's degree in Oncology and Ph.D. degree in Epidemiology & Biostatistics from Peking University. She has led and participated in National Basic Research Program of China "973" and "863", Key International S&T Cooperation Project, National Natural Science Foundation of China, Peking University "985" and "211" Project, and many other programs involving international collaboration. Since 1989, Dr. Pan has participated in a series of epidemiological studies to investigate the risk factors, mechanism, and prevention of gastric cancer in Linqu County, Shandong Province, a high-risk area of gastric cancer in China. Dr. Pan's group has established several endoscopy-based follow-up cohorts and intervention trials in Linqu. Such cohorts are perfectly suited for the identification of biomarkers in gastric preneoplastic lesions, over the course of gastric carcinogenesis. She has published more than 100 papers in peer-reviewed journals, including more than 60 papers in SCI journals.

Yun Peng, MTI
Program Officer, Division of Exchange
Office of International Cooperation
Peking University Health Science Center

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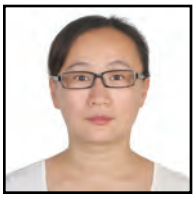
Yun Peng obtained a MTI degree at China Foreign Affairs University. She has been working since 2015 in the Office of International Cooperation, where she is responsible for developing partnerships with universities, scientific research institutions, NGOs, and companies in Europe. She facilitates the visits of international professors, experts, and faculty members.

PKUHSC Delegation

北京大学医学部代表团成员名单



Huiying Qi, PhD
Associate Professor
Department of Natural Science in Medicine
Peking University Health Science Center

Email: qhy@bjmu.edu.cn

Dr. Qi is in charge of Peking University Clinical Research Institute information technology work. She graduated in 1997 with a bachelor's degree and master's in Information Technology from Beijing Normal University. In 2010, she graduated from National Science Library, Chinese Academy of Sciences, with a doctoral degree in Informatics. She is currently responsible for building Peking University Clinical Research Institute's information technology platform and managing information systems such as REDCap and OpenClinica. She is also an Associate Professor in the PKUHSC Department of Natural Science in Medicine. Her research interests are in medical information systems and medical data mining.

Huiying Rao, MD, PhD
Professor of Medicine
Assistant Director, Peking University Hepatology Institute
Vice Director, Scientific Research Department
Peking University Second Hospital

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Huiying Rao is a Chief Physician in Peking University People's Hospital and Peking University Hepatology Institute. She carried out her medical and research training at Peking University Health Science Center before being appointed as Lecturer in Infectious Diseases in 2006. Her research interests are in clinical management of viral hepatitis, cirrhosis, and fatty liver diseases. As the PI of several National Nature Science Foundation of China, Technological Nova of Beijing, and hospital-funded projects, and the primary investigator of a National Science and Technology Major Project for Infectious Diseases Control project, she has carried out several studies focused on the clinical outcome and monitoring of chronic hepatitis B & C, and optimizing treatment of the chronic hepatitis. She has also performed studies on diagnostic markers and new therapy target of hepatitis related cirrhosis and hepatocelluar carcinoma, and the epidemiology, diagnosis and mechanism study of fatty liver diseases. Dr. Rao has published in these research areas in peer-reviewed journals such as the *Journal of Viral Hepatitis*, *Journal of Virological Methods*, *Hepatology*, *Proteomics*, and the *Journal of Gastroenterology and Hepatology*.

Ning Shen, MD
Vice Director, Pulmonary Division
Vice President
Peking University Third Hospital

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Dr. Shen received a medical degree from Beijing Medical University in 1995, with residencies and fellowships in internal medicine and pulmonary and critical care. Since 1995, she has been engaged in clinical, teaching, and scientific research work through the Respiratory Department of PKUHSC Third Hospital, where she has gained rich experience in the diagnosis and treatment of pulmonary infectious diseases, bronchial asthma, COPD, interstitial lung disease, and other diseases of the respiratory system. Skilled in bronchoscopy and thoracoscopy technique, Dr. Shen has focused much of her investigative career on respiratory infectious disease and COPD. In recent years, she has become interested in multidrug-resistant organism infection. She is a member of the Chinese Medical Association of Respiratory Disease Infection Study Group. She was appointed Vice President of PUTH in 2018 and is responsible for education.

北京大学医学部代表团成员名单

PUKHSC Delegation

Jie Shi, MD, PhD
Executive Deputy Director/ Professor,
National Institute on Drug Dependence,
Peking University

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Dr. Shi's research focuses on the neurobiological, molecular genetic, and neuroimaging mechanisms of drug addiction and related psychiatric disorders. She has presided over a number of research projects supported by the National Natural Science Foundation of China, Ministry of Science and Technology of China, etc., and has made important breakthroughs in revealing neural plasticity, cognitive dysfunction, and neuroimaging and genetic characteristics in drug addicts and patients with related psychiatric disorders. She has published over 80 high-level research articles in *Science*, *JAMA Psychiatry*, *American Journal of Psychiatry*, *Biological Psychiatry*, and other top journals in this field. Through her work, Dr. Shi won the Outstanding Achievement Award for Scientific Research in Higher Education Institutions (first prize, Natural Science Award) in 2008 and 2013; the second prize of the Chinese Medical Science and Technology Award in 2008 and 2015. She is the Director of Beijing Key Laboratory of Drug Dependence; the Vice Chairman and Secretary-General of China Expert Committee on Prevention and Control of Drug Abuse; the Vice Chairman of the Committee of Drug Dependence and Abuse, Chinese Society of Toxicology; and the Editor-in-Chief of the *Chinese Journal of Drug Dependence*.

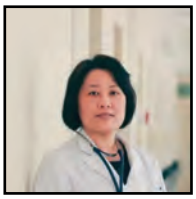
Yu Shi, MD, PhD
Vice Director, Scientific Research Department
Associate Chief Physician of Ultrasound in Obstetrics & Gynecology.
Peking University Shenzhen Hospital

Email: 13823578405@qq.com

Dr. Shi received his PhD in Medical Imaging and Nuclear Medicine from Peking University in 2017 and was selected as visiting scholar to the Miami University Health Center Department of Obstetrics & Gynecology from November 2017 to January 2018. He was involved in the Center for Fetal diagnosis and treatment (prenatal diagnosis center) for almost 10 years. He was mainly involved with ultrasound-guided aspiration, such as percutaneous amniocentesis (1500 cases/year), percutaneous chorion villus sampling (100 cases/year), percutaneous umbilical blood sampling (500 cases/year) and the classic prenatal 3-D ultrasound examination (3000 cases/year). Dr. Shi conducts basic and clinical research with a focus on the roles of prenatal diagnosis ultrasound and the contrast enhanced material microbubble. His research covers the analyzed ultrasound data based on real-world data. In 2012, he reported the targeted delivery of GDNF through the Blood–Brain Barrier by MRI-guided focused ultrasound. In 2016, he reported the classification and prognosis evaluation of fetal vertebral malformation by prenatal 3D ultrasound. In recent years, his research has focused on the big data, especially using machine learning for ultrasound. His team is using deep learning to evaluate the risk rate of ovarian hyperstimulation syndrome during assisted reproductive technology.

PKUHSC Delegation

北京大学医学部代表团成员名单



Yuqin Song, MD, PhD
Associate Professor of Medical Oncology
Deputy Director, Lymphoma Department
President Assistant, Peking University Cancer Hospital

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Dr. Song received her MD degree from Shandong University and a PhD from Peking University Health Science Center. She was trained as a visiting scholar in Nebraska University Medical Center from 2009 to 2010. Today, she is Deputy Director of the Lymphoma Department in Peking University Cancer Hospital (PUCH), the only specified lymphoma center in China with more than 800 new inpatient cases and 25,000 outpatient visits each year. Dr. Song's specialty is the clinical diagnosis and treatment of lymphoma, particularly focusing on clinical trials of novel agents and cellular therapies, such as novel BTK inhibitors, PI3K inhibitors, PD-1 antibodies, CAR T cells in different kinds of lymphoma subtypes. Yuqin Song is the leading PI in PUCH. Yuqin Song also does some basic or translational research involving BTK inhibitor resistance and preclinical research of novel agents. Her research has been supported by the National Science Foundation Committee and the Beijing government. Dr. Song is the General Secretary of Union for China Lymphoma Investigators (UCLI), CSCO; a Vice Chairman of Lymphoma Division, Chinese Geriatric Oncology Society (CGOS); a Vice Chairman of Younger Committee of Lymphoma Division, Chinese Anticancer Association (CACA); and a member of the China Hematological Immunology Society.

Jiazeng Su, DDS
Associate Professor of Oral and Maxillofacial Surgery
Department of Oral and Maxillofacial Surgery
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Dr. Su's research is focused on autologous microvascular transplantation of submandibular gland (SMG) for severe dry eye. His team has treated 191 patients with 207 severe dry eyes, which represents the world's largest number of submandibular gland transplantation cases. More than half of patients experience vision improvement to various extent. Dr. Su used the venous contrast-enhanced computed tomography imaging to predetermine the size of the receipt and donor veins in the temporal region and submandibular gland before operation. This technique helped to reduce the incidence of postoperative vascular and the survival rate of the transplanted SMG was increased. He helped to establish a new system in regulating the salivary secretion of the transplanted submandibular gland. He proposed a standard protocol that employs a combination of capsaicin and carbachol to promote the secretion of transplanted hypofunctional submandibular gland in the first three months after transplantation, which successfully reduced the incidence of duct obstruction. He introduced the concept, diagnostic criteria, and prevention of chronic obstructive sialadenitis of transplanted SMG, and established imaging diagnostic protocols and new methods for functional evaluation, which significantly reduced postoperative surgical complications.

北京大学医学部代表团成员名单

PUKHSC Delegation

Qiudan Sun, MA
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Dr. Sun is the Director of the Office of International Cooperation of Peking University Health Science Center (PKUHSC). Professor Sun also serves as Vice Chair of the Department of Applied Linguistics at the School of Foundational Education, PKUHSC. She is a co-lead for the Collaboration Core for the Michigan Medicine-PKUHSC Joint Institute. Professor Sun's research interests include the science of collaboration and applied linguistics.

Feng Wan, MD
Professor and Chair
Department of Cardiac Surgery
Peking University Third Hospital

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Dr. Wan graduated from Hunan Medical College in 1983, followed by a five-year resident training in cardiovascular surgery and appointment as attending surgeon in 1988 at Fu-Wai Hospital of Chinese Academy of Medical Sciences. He has studied at Paris 12th University, Yale School of Medicine, Oregon Health Science University, and the University Hospital of Western Ontario University. In 1996, he returned to China and was appointed as Chairman and Professor of the Department of Cardiovascular Surgery at Peking University People's Hospital, in Beijing. Dr. Wan has pioneered in many areas of cardiovascular surgery including trans-myocardial laser revascularization (TMLR), off-pump coronary artery bypass (OPCAB), and artificial ventricular assist device (VAD). Prof. Wan established the first western-style, semi-private medical professional service organization (Doctor's Group) in China, a service network that now comprises more than 50 hospitals throughout the country. His contributions and achievements have been widely reported in the *Wall Street Journal*, *Far Eastern Economic Review*, *Discovery Channel*, etc. He was appointed an Academician of National Academy of Surgery of France in 2013.

PKUHSC Delegation

北京大学医学部代表团成员名单

Deli Wang, MD, PhD
Professor of Orthopedics
Director, Bone and Joint
Surgery Department
Peking University Shenzhen Hospital

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Dr. Wang received his MD/PhD in orthopedic medicine from Xi`an Jiao Tong University in 2002 before joining the faculty at PLA Navy General Hospital. In 2017, he was recruited as the Chief of the Bone and Joint Surgery Department at the Peking University Shenzhen Hospital. His particular research field is spine degeneration research with a focus on the roles of stem cells in disc regeneration. In recent years, his group has published many papers in *Stem Cell International*, *Experimental and Therapeutic Medicine*, *Tissue*, and more.

Guisong Wang, MD
Professor & Deputy Director of Cardiology
Peking University Third Hospital

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Dr. Wang completed his medical degree at Peking University Health Science Center. His patient care emphasis is in coronary artery disease, hypertension, dyslipidemia and heart failure. His subspecialty has been focused on coronary angiography and percutaneous coronary intervention (PCI). His research is focused on cardioprotection of remote ischemic conditioning and pharmacological conditioning in basic and clinical settings of ischemic heart disease. His studies in this area has been supported by The National Natural Science Foundation of China and The Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry. In collaboration with Professor Subramaniam Pennathur from Michigan Medicine, he has completed a translational study about dysfunctional HDL and coronary artery diseases. Currently, he is working closely with Professors Bertram Pitt and Stevo Julius on a randomized control trial about different diuretics and target organ damage in patients with hypertension and obesity.

Jianliu Wang, MD
Vice President, Peking University Second Hospital
Chairman and Professor, Department of Obstetrics & Gynecology
Peking University Second Hospital

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Dr. Wang's early publications focused on cervical and endometrial cancer. After a one-year study in Karolinska Hospital (Stockholm, Sweden), his focus shifted to research of female pelvic floor dysfunction disease. He spent 13 years on specific training and expertise in not only female pelvic floor reconstruction practice, but also epidemiology, immune-histochemical and receptor characteristic, tissue biomechanical properties and microstructure abnormality in normal, urinary incontinence and prolapse women, as well as pelvic floor MR imaging analysis and tissue engineering mesh research. In 2006, Dr. Wang's lab began a research collaboration with the Biomechanical Engineering Department of Beihang University in tissue properties. Meanwhile, as the Chairman of the National Center for Pelvic Diseases Control and Beijing Key Laboratory of Female Pelvic Floor Disorders Diseases, he has long-term cooperation with experts in multiple related fields including bioengineering, urogynecology, gastroenterology, radiology, and many more. He documented the initial application of POP-Q staging and pioneer comparison study of polypropylene, allografts, porcine small intestine submucosa and native tissue repair approaches in China. Those demonstrated the different surgical treatments and outcome evaluation of pelvic dysfunctional disease in China.

北京大学医学部代表团成员名单

PUKHSC Delegation

Jingmin Wang, MD
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Dr. Wang's work focuses on clinical and genetic research of brain developmental disorders and related diseases such as intellectual disability/developmental delay and leukodystrophy diseases for which genetic counseling and prenatal diagnosis are performed. She received her PhD from the Beijing Children's Hospital, Affiliated Capital University of Medical Science in July 2002 and finished her postdoctoral research in July 2004 at the PKUHSC. She is the author of more than 50 papers and has received 10 grants as PI from the National Natural Sciences Foundation of China, Natural Sciences Foundation of Beijing, "973" Project of the Science and Technology Ministry of China, and the Michigan Medicine-Peking University Health Sciences Center Joint Institute (JI) for Translational and Clinical Research. Her specific research has included a study of molecular genetics in brain development and related neurogenetic diseases (BDRND); a study on pathogenic mechanisms of two leukodystrophies; research on the mechanisms of early seizure-like injuries; and more.

Tao Wang, MD
Director, Peking University Shenzhen Hospital
Shenzhen High Level Professional and Technical Personnel, Shenzhen Personnel Bureau
State Council Special Allowance, State Council

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Dr. Wang is Secretary of the Party Committee of Peking University Shenzhen Hospital. He has served as Chief Physician in Cardiovascular Surgery of Peking University Shenzhen Hospital. As a well-known expert in the field of pediatric cardiovascular surgery in China, Dr. Wang has rich experience and unique insight in the diagnosis and treatment of neonatal and infant congenital heart disease and critical care treatment. He successfully helped establish two cardiovascular centers in Qingdao and Shenzhen and has treated more than 3000 cases of congenital heart disease with a 99.3% success rate; the success rate of the critical complex congenital heart disease below 6 months is 96.8%. The first cold autologous blood cardioplegia solution was first used in the protection of cardiopulmonary bypass in children. A series of animal experiments and clinical studies were carried out with more than 1000 clinical cases were applied. The clinical effect was similar to that of HTC solution, which was the best in the international recognized myocardial protection, and the cost was only 1% of the HTC solution. His current interest is in medical education with a focus on the treatment of lung cancer.

PKUHSC Delegation

北京大学医学部代表团成员名单

Weimin Wang, MD, PhD
Professor of Surgery
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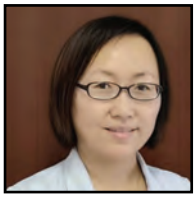
Dr. Wang is the Vice President of Peking University Health Science Center, the head of Institute of Medical Education of Peking University, and the Director of Medical Education Department of PKUHSC. He also serves as executive member of the deputy secretary-general of the Medical Education Committee of China Association of Higher Education; Vice President of the Teaching Management Council of the Medical Education Committee of the Chinese Association of Higher Education; the Deputy Secretary-General of the Working Committee for the Accreditation of Medical Education of Ministry of Education; Vice Director of Research Center for Clinical Medical Education of Ministry of Education; Secretary-General of the Teaching Steering Committee of Clinical Medicine of Ministry of Education; and Vice Chairman of the Teaching Working Committee of Clinical Medicine of Ministry of Education. In addition, Dr. Wang is head of the Branch of Portal Hypertension in Chinese Society of Surgery of Chinese Medical Association; Vice Chairman of the Branch of Biliary Tract Surgeon in Chinese Medical Doctor Association, Standing Committee; and Deputy Secretary-General of the Chinese Society of Medical Education.



Xiaoyan Wang, MD, PhD
Professor & Director, Department of
Operative Dentistry & Endodontology
Peking University School & Hospital
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Dr. Wang is a committee member of Chinese Society of Cariology and Endodontology, and the Beijing Society of Cariology and Endodontology. She leads both clinical and basic research focused on Operative Dentistry & Endodontology and dental materials and has published more than 70 peer-reviewed papers. Her current key interests include: the development of dental biomaterials (e.g., smart materials for sustained and control release, pH-responsive materials, antibacterial materials; repair and enhancement of teeth (e.g., bio-remineralization, dental adhesives, polymer-based restorative materials); and regenerative dentistry (e.g., pulp regeneration scaffold material, injectable hydrogel for bone repair).

北京大学医学部代表团成员名单

PUKHSC Delegation

Yanfang Wang, MD, PhD, MS, MHSc
Professor and Associate Director
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Peking University Clinical Research Institute is a comprehensive research center for all clinical research at PKUHSC. After working in the US for more than 20 years, Dr. Wang joined the Institute in 2008 as the first full-time employee. She is experienced in population epidemiological studies and clinical trials, and has worked in several large population and clinical epidemiological studies. Her current research projects include: the PKUHSC-Duke collaboration study focusing on Weight Loss Using New Media Strategies among Adults in Beijing; Joint Project with Peking University 2nd Hospital on Establishing an ECG database for Chinese Population in China (funded by the 3rd phase of Peking University 985 Project); Joint Project by Clinical Hospital and Basic Science Research; and a population study on metabolic disease and non-alcohol fatty liver disease in the Pinggu District, Beijing China. Dr. Wang is also a co-lead for the Bioinformatics and Biorepository Core in the JI collaboration between PKUHSC and Michigan Medicine.

Lai Wei, MD, PhD
Director and Professor of Peking University
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Dr. Wei's research has focused on the natural course and treatment of chronic hepatitis B and C, exploring risk factors for disease progression including fibrosis and hepatocellular carcinoma. Previous work involved both bench and clinical studies on hepatitis B, hepatitis C, and metabolic disorder. More recently, as a PI supported by a central government grant, he is in charge of a nationwide collaborative study on long-term follow-up and treatment optimization of hepatitis C since 2008.

Dr. Wei has contributed to three versions of the Asian Pacific Association for the Study of the Liver Guidelines on HCV (2007-2014) and the organization's Guidelines on HBV (2015). He also contributed original data on the etiology of liver cirrhosis, and epidemiology, natural history of chronic HCV infection in China, factors associated with HCV-related cirrhosis, and treatment strategies for hepatitis C. Dr. Wei also explored hepatic steatosis and metabolic abnormalities in hepatitis patients, including association of stages of fibrosis and HBV DNA in hepatitis B patients with hepatic steatosis. He has collaborated with U-M Professor Anna Lok since 2010, publishing three papers together to date. In late 2013, they secured external funding to support an ongoing JI study on hepatitis C through end of 2018. Their current work is on non-alcoholic fatty liver disease (NAFLD) research.

PKUHSC Delegation

北京大学医学部代表团成员名单

Jianmin Wu, PhD
Professor of Bioinformatics
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Dr. Wu is a senior bioinformatician focusing on data-driven cancer research, which combines high-throughput genomic, transcriptomic and proteomic profiling approaches, to comprehensively investigate molecular landscapes of GI cancer and identify prognosis/predictive biomarkers and novel therapeutic targets. He published 40+ publications in peer-reviewed journals with more than 2000 citations, including corresponding author work in *Nature Methods*, *Nature Reviews Cancer* and *Nucleic Acids Research*, as well as collaboration work in *Nature* and *Cell*. Dr Wu did his postdoctoral research at Biomedicum Helsinki (Finland, 2006-2010) and has been a group leader at Garvan Institute of Medical Research (Australia, 2010-2015), where he started involvement in the International Cancer Genome Consortium (ICGC) pancreatic cancer project by contributing to the functional and integrative analysis. In early 2016, Dr. Wu moved back to Beijing and established the Center for Cancer Bioinformatics at Peking University Cancer Hospital. He is also a member of the ICGC-ARGO Scientific Planning Committee.

Jing Wu, MD
Associate Chief Physician
Department of Radiology
Peking University Second Hospital

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Dr. Wu has been working in the radiology department of Peking University Second Hospital since 2000. Her research interest has been pelvic floor function imaging diagnosis. In the past few years, she has been involved in the Magnetic Resonance Imaging research about levator ani injury and pelvic floor changes of women with pelvic organ prolapse. Further studies will be conducted in the MR evaluation of surgical recurrence and postpartum recovery in patients with pelvic floor prolapse and maternal. Dr. Wu is also interested in MR screening for breast cancer and has worked with the Breast Center for this part of the study. The team explored the clinical feasibility of screening breast cancer with an abbreviated protocol of breast magnetic resonance imaging (BMRI-AP) and found BMRI-AP with shorter acquisition time and interpretation time has similar ability in detection and diagnosis of breast cancer compared with full diagnostic protocol BMRI (BMRI-FDP). BMRI-AP was demonstrated as an efficient imaging tool in screening breast carcinoma.

Ping Wu, MD, PhD
Director Assistant
Associate Professor
National Institute on Drug Dependence
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Dr. Wu's research focuses on neurobiological mechanisms and clinical intervention of pathologic memories and related disorders, especially the non-pharmacological intervention of addiction memory. Dr. Wu demonstrated the effect of conditioned or unconditioned stimulus-induced retrieval-extinction procedure in heroin and methamphetamine addicts. She is now undertaking projects supported by the National Natural Science Foundation, Science and Technology Ministry of China. She has published more than 30 SCI papers in journals such as *Science*, *JAMA Psychiatry*, *Biological Psychiatry*, *Journal of Neuroscience*, and *Psychopharmacology*. Her research has been awarded an Outstanding Achievement Award for Scientific Research in Higher Education Institutions, Chinese Medical Science and Technology Award. Dr. Wu is a reviewer of *Neuropsychopharmacology*, *Psychoneuroendocrinology*, *Drug and Alcohol Dependence*, *Psychoneuroendocrinology* and *PLoS One*.

北京大学医学部代表团成员名单

PUKHSC Delegation

Song Wu, MD
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Dr. Wu studied at Peking Union Medical College and Fuwai Hospital under Professor Liu Ying-long to earn his doctorate in cardiac surgery in 2007 and began working at Peking University Third Hospital in 2010. As Deputy Chief Physician of Cardiac Surgery, he leads a medical team engaged in surgical treatment of coronary heart disease, valve disease, congenital heart disease, and aortic artery disease. He is good at the installation and management of the extracorporeal membrane oxygenation (ECMO); he specializes in handling critical illness after cardiac surgery and management of the intra-aortic balloon counterpulsation (IABP), continuous hemofiltration (CRRT), neonatal and infant peritoneal dialysis, and the bedside percutaneous dilatation tracheotomy (PDT). Dr. Wu is the author of 18 publications, including 2 SCI articles. He holds eight national utility model patents.

Yangfeng Wu, MD, PhD
Executive Director
Peking University Clinical Research Institute
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Dr Wu's research focuses on practical measures in the prevention and control of cardiovascular disease. He developed the Chinese prediction model of 10-year risk of cardiovascular disease and led the working group to develop the Practical Guidelines for Prevention and Treatment of Hypertension in Primary Care. He has co-authored several guidelines for the prevention and treatment of cardiovascular diseases and has published more than 260 academic papers in Chinese and international academic journals. In 2009, he set up the International Centre for Chronic Disease Prevention in China jointly with 12 academic institutions at home and abroad. In 2013, under his leadership, China's first program of Sciences in Clinical Research was established under the approval of the Ministry of Education of China to train graduate students for conferment of master's degrees and doctorate degrees.

Han Xiao, MD, PhD
Associate Professor of Medicine
Institute of Vascular Medicine
Peking University Third Hospital

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Dr. Xiao received her MD/PhD from Peking University on 2008 and continued her postdoctoral work at University of California, Riverside, from 2010-2012. Her primary interest is on inflammation and cardiovascular disease with two major research goals: (1) to understand the role of inflammation in cardiac and vascular remodeling; and (2) to develop novel therapeutics strategy for cardiac and vascular remodeling. In a series of publications, her work identified inflammasome as the common anti-inflammatory target for cardiac and vascular remodeling. She also investigated the underlying mechanisms of metformin against cardiac inflammation and fibrosis using multidisciplinary methods. As the first author or corresponding author, she has published several papers on the famous journals including *European Heart Journal*, *Circulation*, *Cardiovascular Research*, and the *British Journal of Pharmacology*. She obtained the National Science Fund for Outstanding Young Scholars in 2018 and the CNPHARS-SERVIER Young Investigator Awards in pharmacology in 2017.

PKUHSC Delegation

北京大学医学部代表团成员名单

Yu Xiao, MPA
Research Associate
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Ms. Xiao received her master's in public administration from the School of Humanities and Social Sciences, Beihang University, in 2014. In her current role, she is responsible for the management of scientific research projects, such as the National Natural Science foundation of China (NSFC), Beijing Science and Technology Commission projects, research projects from government ministry, and also one of management team members of the Michigan Medicine – Peking University Health Sciences Center Joint Institute for Translational and Clinical Research (JI) project. Her own research analyzing the distribution and achievements of the Science Foundation for Youth undertaken by female scientists at PKUHSC revealed the importance of the Science Foundation for Youth in the development of female scientists. She has also conducted research and analysis to improve the quality of scientific publications and how to optimize funding process management.

Ana Xie, MA
Associate Director
Office of Medical Education
Peking University Health Science Center

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Ms. Xie is the Associate Director of the Office of Medical Education of Peking University Health Science Center. She also serves as the Director of the Office of the Working Committee for the Accreditation of Medical Education of Ministry of Education; and Vice Director of Institute of Research of Medical Education of Peking University Health Science Center. She has engaged in medical education management for nearly 10 years. Her research interest focuses on medical education evaluation with several published papers about medical education accreditation and evaluation.

Bing Xie, MD
Department of Obstetrics and Gynecology
Peking University Second Hospital

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As a fellow of Obstetrics and Gynecology Department and the Peking University Female Pelvic Center, Dr. Xie is focused on urogynecology both in clinical practice and research study. She is interested in the assessment and therapy of pelvic floor dysfunction disease using MRI. For example, dynamic MRI imaging analysis, 2-D images measurements, 3-D modeling quantification and biomechanical model analysis in anterior vaginal wall prolapse woman, and also pilot study of diffusion tensor imaging (DTI) and fiber tractography for evaluating the integrity of levator muscle fiber before and after delivery. She spent more than year at U-M as a visiting scholar working in PFRG furthering her work on rectocele size measurement and 3D pelvic floor modeling.

北京大学医学部代表团成员名单

PUKHSC Delegation

Gaoqiang Xie, MD, PhD
Associate Professor of Clinical Research Methodology
Executive Director, Department of Data Management
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Dr. Xie has undertaken more than 10 studies as a Principal Investigator, sponsored by National Natural Science Foundation of China, Ministry of Science and Technology of China, etc. His research focuses on prevention of cardiovascular diseases in adults, including four themes: studies on quality of life in China; genome-wide association studies of cardiovascular diseases; studies on susceptible genes and environmental risk factors of cardiovascular diseases; and clinical researches on lowering lipid therapy. He has published 50 peer-reviewed academic papers, including 11 papers in peer-reviewed international journals. In addition, Dr. Xie has made great efforts to develop data management platforms in accordance with international standardization. In the past 10 years, he has been devoted to importing, assimilating, and applying Medidata Rave and REDCap electronic data capture (EDC) systems in a series of large clinical research projects. During the period, he led the creation of a series of SOP and guidelines in international data management.

Guangkuan Xie, PhD
Assistant Professor of Medical Ethics
Department of Medical Ethics and Legal Issues
Peking University Institute of Medial Humanities

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Dr. Xie teaches medical ethics, bioethics and public health ethics. He was formerly the Director of Academic Planning Office of Peking University, and was a junior researcher of UC San Francisco(2004-2005); a senior fellow at the University of Minnesota(2011); and a visiting scholar at UC Berkeley(2012). His research interests include medical professionalism, conflict of interests, doctor-patient relationships, medial humanity education, and higher education administration.

PKUHSC Delegation

北京大学医学部代表团成员名单

Liying Yan, PhD
Professor of Reproductive Medicine
Associate Director
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Dr. Yan's research has focused on the mechanisms of early embryo development and preimplantation genetic diagnosis. Her major academic achievements include establishing comprehensive gene expression profiles of the human pre-implantation embryos, hESCs, and fetal germ cells, and identifying the key genes regulating embryo development; providing insights into the critical features of the methylome of human early embryos and primordial germ cells, as well as its functional relation to the regulation of gene expression; and constructing the first female personal genetic map by sequencing the polar bodies (PB1 and PB2) and the oocyte pronuclei, demonstrating that maternal genome information could be deduced by the two polar bodies including point mutation and aneuploidy. This has a great impact on the clinical diagnosis of genetic diseases. Dr. Yan developed a new pre-implantation diagnosis method for single gene disorders and applied to the clinic resulting in 52 offspring births. As the first (or co-first) or corresponding author, Dr. Yan published 22 SCI papers (total impact factor of 252) and has been cited 912 times. The highest single-paper citation is 326 times. She has been supported by four NSFC grants, including a fund for Excellent Young Scholars. She obtained two National Science and Technology Progress Awards of China (second class) – in 2017 as the third awardee and in 2011 as the forth awardee.

Ence Yang, PhD
Asst. Professor of Computational Biology
Professor of Microbiology
Institute of Systems Biomedicine
Department of Microbiology
School of Basic Medical Sciences
Peking University Health Science Center

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Dr. Yang has a BSc in Life Sciences from Peking University in 2003, and completed his PhD at the Institute of Microbiology, Chinese Academy of Sciences. During 2011-2015, he received postdoctoral training in computational systems biology at Texas A&M University. In October 2015, he was appointed tenure-track Assistant Professor at the School of Basic Medical Sciences, Peking University Health Science Center. The research of Dr. Yang's group focuses on genetic architecture and adaptive evolution of complex traits/diseases, including deciphering circRNA expression variation in schizophrenia, to develop new sequencing strategy for fungal microbiome, and to unravel evolutionary mechanisms of dimorphism in pathogenic fungi. Dr. Yang also organizes a series of courses in Programming in Bioinformatics for the new PKUHSC-UM Dual Master's Program; directs a full-length course on Computational Biology for Systems Biomedicine Doctor's Program; and lectures various courses for both undergraduate and graduate students. He received the Teaching Awards from PKUHSC in 2017 and 2018.

北京大学医学部代表团成员名单

PUKHSC Delegation

Fan Yang, MD, MSc
Vice Director, Professor of Thoracic Surgery
Peking University Second Hospital

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Dr. Yang received his MD degree at Peking University followed by a post-doctoral fellowship in Tulane University. He finished residency training at Peking University First Hospital and became an attending in Peking University People's Hospital in 2009. He has been a visiting scholar in various top-rated hospitals in the United States including Cleveland Clinic, Mayo Clinic, MD Anderson, and Memorial Sloan-Kettering Cancer Center. His clinical interests include sublobar resection for early lung cancer, fluorescent aided thoracoscopy, adjuvant and systemic therapy for lung cancer. His research focus includes lung cancer proteomics, metabonomics, ctDNA signature for early diagnosis, and all other lung cancer related topics. He is the Youth Secretary-General of Chinese Society of Thoracic and Cardiovascular Surgery.

Hongyu Yang, MD, PhD
Professor of Oral and Maxillofacial Surgery
Academic Leader, Stomatology Center of Peking University Shenzhen Hospital Guangdong Province
Director, Engineering and Technology Research Center for Oral Disease Diagnosis & Treatment, Shenzhen
Director, National Clinical Medical Research Center for Oral Diseases

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Dr. Yang received his PhD in Oral and Maxillofacial Surgery from Wuhan University followed by three advanced trainings in the Department of Maxillofacial Surgery of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University (2003), Center of Craniomaxillofacial Surgery, University Hospital of Zurich and Department of Head and Neck Oncology (2007), and the Cancer Research Institution, Japan (2012). He has engaged in clinical work of oral and maxillofacial surgery for 27 years, specializing in combined radical surgery and reconstruction of postoperative tissue defect of oral cancer (such as tongue reconstruction, jaw reconstruction, etc.), treatment of maxillofacial hemangioma, vascular malformation, and lymphatic malformation. He is proficient in microsurgical techniques and can perform the resection surgery of carotid body tumors. His research fields are mainly in immunology, etiology of oral cancer, and non-coding RNA regulation in oral cancer. His team discovered that LncRNAs such as MALAT-1 and UCA-1 play crucial roles in oral squamous cell carcinoma (OSCC) progression. Moreover, by comparing the expression of CircRNAs in OSCCs and their adjacent normal tissues from patients, Professor Yang's team found serval CircRNAs abnormally expressed in OSCC.

Ming Yang, MD
Associate Chief Physician
Peking University Hepathology Institute
Peking University Second Hospital

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Dr. Yang's research interests are in clinical management of viral hepatitis, cirrhosis, and autoimmune and drug-induced liver diseases. As the investigator of several National S&T Major Project for Infectious Diseases Control projects, she has carried out studies focused on the clinical outcomes and monitoring of chronic hepatitis C and B. She has also performed studies on diagnostic markers for hepatitis C-related cirrhosis and hepatocelluar carcinoma, and on the gap of liver disease care between the United States and China as well as between urban and rural China. Dr. Yang has received funding from the NIH and has published results in peer-reviewed journals such as the *Journal of Gastroenterology and Hepatology*, *Digestive Disease and Scince*, and *Alimentary Pharmacology & Therapeutics*.

PKUHSC Delegation

北京大学医学部代表团成员名单

Qimin Zhan, PhD
Executive Vice Present
Peking University
President
Peking University Health Science Center

Dr. Zhan is an Academician of the Chinese Academy of Engineering, the Executive Vice President of Peking University; President of Peking University Health Science Center; and the Director of the State Key Laboratory of Molecular Oncology.

Dr. Zhan was the Chairman of the National Advisory Board for 863 High-Tech plan in the field of biomedical sciences and is the Chief Scientist of the 973 National Fundamental Program. His research interest is focused on the molecular pathways involved in the control of cell cycle checkpoint and apoptosis after DNA damage, and the signaling pathways involved in regulation of the maintenance of genomic stability and tumor metastasis. In recent years, Dr. Zhan has paid great attention to the cancer translational study, including molecular diagnosis and personalized therapy. His research has successfully attracted multiple grants from different funding agencies. Dr. Zhan has published more than 240 peer-reviewed SCI papers. Many of his publications are in prestigious journals, including *Nature*, *Cell*, the *Journal of Clinical Investigation*, and others. To date, they have been cited more than 14,000 times.

Nannan Zhang, PhD
Research Assistant
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Dr. Zhang earned her bachelor's in biological science and medical engineering at Beihang University in 2011 and studied biology at the Tsinghua University Medical School, earning her PhD in 2016. She was a visiting student at the Harvard Medical School Department of Genetics during her doctoral study period. Her graduate research focused on aging, including a project describing the crucial role of SIRT6 in aging, inflammation and apoptosis regulation. In the Office of Scientific Research Office, her primary responsibility is basic research project management, including the National Natural Science Foundation (NSFC), Beijing Science and Technology Commission projects, etc.

北京大学医学部代表团成员名单

PUKHSC Delegation

Ning Zhang, PhD
Vice President
Peking University Health Science Center

Dr. Zhang obtained his BS in Chemistry and MS in Biochemistry and Molecular Biology from University of Georgia, and a PhD from Johns Hopkins University. He received his postdoctoral training in Laboratory of Molecular Immunoregulation, National Cancer Institute, Supervised by Dr. J. Oppenheim. Dr. Zhang currently serves as the Vice President of Peking University Health Science Center, where he is responsible for academic research. He has been engaged in biomedical and cell biology research for many years. Focused on tumor metastasis, his researches involves the mechanism study, biomarker identification, drug screening, and the application of nanotechnology. Dr. Zhang has received many awards for his achievement in cancer research, including Young Science and Technology Innovation Talents from Ministry of Science and Technology, Distinguished Young Scholar Awards from Nature Science Foundation, Chief Scientist of National Program on Key Basic Research Project (973), New Century Excellent Talents from Ministry of Education, Distinguished Professor of Tianjin, and Excellent Achievement Award from Lee's Foundation.

Hongyu Zhang, MD, PhD
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Associate Professor
Peking University Shenzhen Hospital

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Dr. Hongyu Zhang has been a hematologist for about 24 years. He received his MD from Huazhong University of Science and Technology, Tongji Medical College in 1998 and PHD from Peking University in 2007. He has been working in Peking University Shenzhen Hospital as a hematologist since 1998 and became the chief physician in 2016. His hematology department holds more than 50 beds and receives 300-plus newly diagnosed leukemia and lymphoma patients per year. In each year, his team completes about 30 cases of allo-HSCT for leukemia patients. Dr. Zhang's research primarily focuses on hemapoietic stem cell transplantation (HSCT) and lymphoma. He is now in charge of HSCT in Peking University Shenzhen Hospital and leads several projects related to late-onset hemorrhagic cystitis post allo-HSCT, and immune-reconstitution after allo-HSCT. With respect to lymphoma, he is now working on EBV-associated lymphoma, which is common in southern China. In 2015, CART cell therapy was approved by Hospital Ethics Committees for Hematology Malignancy. To date, his department has completed CART cell therapy in eight cases of refractory B cell lymphoma and one case of multiple myeloma.

PKUHSC Delegation

北京大学医学部代表团成员名单

Lianhai Zhang, MD
Chief Surgeon & Associate Professor
Department of Gastrointestinal Surgery
Peking University Cancer Hospital
Beijing Institute for Cancer Research

Email: zlhzlh@hotmail.com

Dr. Zhang's earned his MD at Fudan University in 2001 and completed in a postdoc in Biochemistry at the University of Texas Southwestern Medical Center in 2002. His research interests mainly focus on surgical oncology in gastrointestinal (GI) cancer and cancer biobank. Recent projects include conducting preclinical trials with ex vivo patient-derived xenografts (PDX) to identify biomarkers which can predict efficacy of drugs; biomarkers identification for patient prognosis and treatment outcome prediction, based on sample analysis in biobank; and constructing and managing a cancer biobank. Dr. Zhang has published two books on protocols and comprehensive management of biobanks in China. He is also an active member of Scientific Program Committee of International Society for Biological and Environmental Repositories (ISBER).

Wei Zhang, MD, MS, PhD
Research Assistant
Peking University Hepatology Institute
Peking University Second Hospital

Email: jiesuifanny@163.com

Dr. Zhang's research interests are in the epidemiology and natural history of non-alcoholic fatty liver disease (NAFLD) in China; extrahepatic manifestations of HCV infection Hepatitis C virus (HCV) infection; and stem cell therapy in fibrosis/cirrhosis. In recent years, she and her colleagues have conducted five systematic reviews and meta-analysis involving hyperglycaemia and HCV, stem cell therapy in end-stage liver diseases, HCV and Hepatocellular Carcinoma, and the prevalence of NAFLD in Asia. Her work has been highlighted at annual meetings of the American Association for the Study of Liver Diseases (2011, 2013), and a paper was published in *PLOS ONE* (2012). Since 2012, Dr. Zhang has explored the prevalence and characteristics of NAFLD patients in Beijing. She has finished a cross-sectional survey with randomized multistage stratified cluster sampling and is now working on analyses and manuscript preparation. Dr. Zhang is the project manager for a JI-funded project: The Role of Visceral Adiposity in the Pathogenesis of Non-Alcoholic Fatty Liver Disease (NAFLD) in Lean versus Obese Patients: A Comparative Study between Patients at Michigan Medicine versus PKUHSC. She recently spent more than a year at U-M as a visiting scholar in Gastroenterology and Hepatology.

Xiaotian Zhang, MD, PhD
Professor & Chief Physician, Department of Gastrointestinal Oncology
Deputy Director, Teaching and Research of Medical Oncology
Deputy Director, Office of International Affairs, Peking University Cancer Hospital

Email: zhangxiaotianmed@163.com

Dr. Zhang obtained her doctor's degree in oncology from Peking University School of Oncology in 2006 and has worked in the Department of Gastrointestinal Oncology at Peking University Cancer Hospital since 2000, focusing on diagnosis, medical treatment of and research of GI cancer. She is an expert in standardized treatment of advanced gastric cancer and nutrition support for cancer patients. She participated in the formulation of several relevant national and international guidelines, including the National Health Commission standards for diagnosis and treatment of gastric cancer. Dr. Zhang's clinical and translational research focuses on issues in clinical practice, especially for advanced gastric cancer. She has participated in over a dozen international and domestic multi-center clinical trials. As the local PI, she is now leading implementation of several Phase II and III clinical trials on the first- and second-line treatment for gastric cancer. As the coordinator, she is in charge of the design, implementation, quality control and evaluation of a large-sample multi-center Phase III randomized trial (PACC of advanced gastric cancer) and two large-scale, domestic, multi-center Phase III randomized trials (RESOLVE and RESOLVE2 for locally advanced gastric cancer).

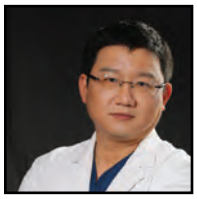
北京大学医学部代表团成员名单

PUKHSC Delegation

Xuehui Zhang, PhD
Associate Professor
Department of Dental Materials
Peking University School and Hospital of Stomatology

Email: zhangxuehui@bjmu.edu.cn

Dr. Zhang earned his PhD degree from Jilin University in 2012 and was a Postdoctoral Fellow at the College of Materials Science and Engineering, Tsinghua University (2012-14). He is now serving as Associate Research Fellow and Master's tutor in the Department of Dental Materials, Peking University Stomatological Hospital. Dr. Zhang was the winner of the 2016 Young Elite Scientist Sponsorship Program by China Association for Science and Technology (CAST). Dr. Zhang is the Reviewer of international scientific journals including Biomedical Materials, Applied Surface Science, etc. He is also the project leader of the National 863 sub-project, National Natural Science Foundation, Young Elite Scientist Sponsorship Program by CAST. His primary research interest is the functional design and performance evaluation of bone replacement materials for bone and dental restoration. Dr. Zhang has published 34 papers in scientific journals, including 16 papers as first or corresponding author, and holds three national innovation patents.



Yan Zhang, MD
Professor of Cardiovascular Medicine
Department of Cardiology
Peking University First Hospital

Email: drzhy1108@163.com

Dr. Zhang graduated from Peking University in 2001 with an MD and received four years of postdoctoral research training at the Harvard School of Public Health. Dr. Zhang is currently serving as more than 10 social positions in China, such as member of the Cardiovascular Precision Medicine Group of the Chinese Society of Cardiology (CSC); member of the Prevention and Control Committee for Heart Disease of the Chinese Preventive Medicine Association; Vice President of the Cardiovascular Disease Committee of the China Non-government Medical Institutions Association, etc. His research interests are mainly focused on the epidemiology, genetic study, and clinical research management of cardiovascular diseases. He leads a community-based arteriosclerosis cohort study in Beijing which aims to observe the relationship of inflammatory biomarkers, metabolic biomarkers, atherosclerotic indicators, and genetic factors with atherosclerosis and hypertension. Dr. Zhang is also in charge of two genetic projects supported by the Joint Institute, one on blood pressure and another on hematologic traits. He has authored more than 50 publications in peer-reviewed journals.

PKUHSC Delegation

北京大学医学部代表团成员名单

Zhe Zhang, MD
Vice Director of Cardiac Surgery
Peking University Third Hospital

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Dr. Zhang's basic research interests focus on the gene polymorphism and the role of PPAR-α/γ agonist in endothelial function in patients with or without diabetes. He and his team have shown that coronary flow velocity reserve is significantly improved by fenofibrate treatment in patients with hypertriglyceridemia. In addition, the plasma level of Hcy was significantly increased with fenofibrate treatment as compared with baseline levels. These data indicate that fenofibrate may help protect against atherosclerosis by promoting the re-coupling of endothelial NO synthase with increased levels of BH4 and normalizing endothelial disorders. This endothelial protective effect may be reduced in part by increasing the HHcy effect.

Since 2006, Dr. Zhang has undertaken research projects funded through the Chinese National Natural Science Foundation, Capital Medicine Development Foundation, and more. He also took part in a few scientific projects, such as Major National Basic Research Program of China and PKU-UM project about acute aortic dissection. Today, he is the Director of the Heart Failure program in the Cardiac Surgery Department and remains very interested in the surgical treatment and basic research of acute and chronic heart failure.

Shuguo Zheng, DMD, PhD
Professor and Chairman
Department of Preventive Dentistry
Peking University School and Hospital of Stomatology

Email: kqzsg86@bjmu.edu.cn

Dr. Zheng graduated from the School of Stomatology, Beijing Medical University with a DMD degree in 1992 followed by a PhD degree in 1996. As a postdoctoral fellow or a visiting scholar, he worked in Germany (1997), Nihon University (1999), Hong Kong University (2003), and King's college University of London (2007). In 2003, he passed the examination of Royal College of Surgeons of Edinburgh and became the first scientist from the mainland of China elected as the M Paed Dent RCS (Edin., UK). He is the second director and the office director of the World Health Organization Collaborating Center (WHOCC) for the Research and Training in Preventive Dentistry in China, and is also the Vice Secretary-General of China Oral Health Foundation as well as the Chairman of the Stomatological Society of Chinese Association for Improving Birth Outcome and Child Development. His research focuses include molecular biological study for the dental developmental abnormality (esp. CCD and Hypodontia); molecular epidemiological study and biomarker study for dental caries and periodontal disease; and the study of the policy for dental public health in China. He has received more than 16 national research grants in China and published more than 70 papers in journals such as *JDR*, *JCP*, *Caries Research* and *Mutagenesis*. Serving as a Key National Stomatological Expert for the National Health Commission of the People's Republic of China, he participates in the design and management of the national dental prevention programs and the formulation of national dental public health policy.

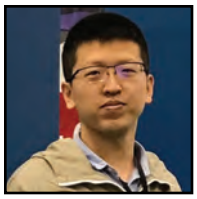
北京大学医学部代表团成员名单

PUKHSC Delegation

Ya'an Zheng, MD
Professor of Emergency Medicine
Chief Director, Department of Emergency Medicine
Peking University Third Hospital

Email: z.y.a@medmail.com.cn

Dr. Zheng graduated from Capital Workers Medical College in 1979 and has worked in the Peking University Third Hospital Emergency Department since 1986. He is a Chief Physician and Chief Director of Department of Emergency Medicine since 2003. His past research work focused on pulmonary embolism / acute coronary syndrome /COPD. In recent years, he has explored therapeutic hypothermia for cardiac patients after resuscitation and ECPR. He is actively involved in implementing clinical research projects in the Emergency Department and is the principle investigator of the JI project: Rapid bacterial identification and antibiotic susceptibility testing in patients with sepsis by chiroplasmic nanorod PCR (NR-PCR). Dr. Zheng is an instructor of the American Heart Association, BLS and ACLS training since. He is also a member of the expert group of advanced simulation training of Sino-French cooperation Medical Center for Emergency and Disaster. He is a member and General Secretary of the Eighth Committee of Emergency Medical Association of Chinese Medical Association; Deputy Director of the Eighth Committee of Emergency Medical Branch of Beijing Medical Association; and a member of the Emergency Medical Branch of the Chinese Medical Doctor Association. He has served as Chief Translator for two Oxford Handbooks on emergency and acute medicine.



Jingcheng Zhou, MD
Department of Urology
Peking University First Hospital

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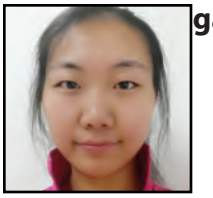
Dr. Zhou is interested in the pathogenesis of renal cell carcinoma and bladder cancer. His research experience has involved some genes and their related signal pathways about the two kinds of cancers. For the mechanism of bladder cancer, he has found a gene named KPNA2 associated with nuclear transportation of OCT4 and effect multiple cancer cell behaviors afterwards. He also focused on the function of a novel gene named MGC45491 in renal cell carcinoma, and revealed the relationship between hypoxia and this gene. Since 2012, Dr. Zhou and his colleagues have explored the function of immunotherapy targeting erythropoietin receptor (EPOR) and successfully produced anti-EPOR polyclonal and monoclonal antibodies. Also, they have demonstrated that anti-EPOR polyclonal antibody not only has high affinity for EPOR but also can block the EPO-EPOR pathway to inhibit proliferation of renal cell carcinoma cell lines. In addition, through in vivo experiments, anti-EPOR polyclonal antibody also significantly inhibited renal cell carcinoma xenografts' growth on nude mice. Based on the above results, we continue to improve the antibody therapeutic efficacy and lay the foundation for the research of functions of humanized monoclonal antibody and anti-EPOR CAR-T cells.



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Shiwei Zhou, PhD Postgraduate
Department of Gastroenterology
Peking University Third Hospital

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Ms. Zhu is a PhD postgraduate and Research Assistant in Prof. Liu Dong Yan's group at the Peking University Third Hospital Department of Gastroenterology. Shiwei has broad interests in the genetic, diet and mental disorder influence on functional gastroenterology diseases and their interaction. Her research is mainly focused on interaction of gut microbiota and irritable bowel syndrome through the brain-gut axis.

Xiaohui Zhu, MS
Research Associate, Reproduction Key lab
Lab Manager, Department of
Reproduction Center
Peking University Third Hospital

Email: 13611376749@163.com

Ms. Zhu has been a Research Assistant and Lab Manager in Dr. Qiao's Lab in the Reproduction Center of Peking University Third Hospital since 2013. Before that, she had been in a similar position at University of Texas Southwestern Medical Center for several years. Ms. Zhu has published 27 SCI papers as a first or co-author. Currently, as PGD technical supervisor in Peking University Third Hospital Reproduction Center, she is in charge of the single gene PGD (embryo preimplantation genetic diagnosis) technique group, including PGD patient's process management. So far, the PGD group accomplished embryo diagnosis for 209 cases (277 cycles) out of total 400 PGD cases. In all, 53 PGD offspring have been born. The other contribution of Ms. Zhu is management of the Reproduction Key lab which has 10 principal investigators, 9 post doctors, and 55 PhD students. The lab is focused on reproduction basic research and clinical transformation. The routine management duty is including personnel management, funds management, instruments and equipment management etc.

U-M Participants

密西根大学发言人名单

Hasan B. Alam, MD
Norman W Thompson Professor of Surgery
Section Head of General Surgery

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Dr. Hasan is an Acute Care Surgeon who is certified by the American Board of Surgery in General Surgery and Surgical Critical Care. He received his surgical training at the Washington Hospital Center in Washington DC, followed by a post-doctoral research fellowship at the Uniformed Services University of Health Sciences (USUHS) in Bethesda, MD. He then served as a faculty member at the Georgetown University as well as USUHS before moving to Boston to join the Massachusetts General Hospital (MGH) in 2005. There he was rapidly promoted to the position of Professor of Surgery at the Harvard Medical School, and served as the Director of Surgical Critical Care Fellowship Program at the MGH. He was also the founding Medical Director of the multi-disciplinary Intensive Care Unit, and chaired the State Committee on Trauma for many years before moving to Ann Arbor in 2012. Dr. Alam's clinical interests are in the areas of trauma, emergency general surgery and surgical critical care. His research focuses on hemorrhagic shock, traumatic brain injuries, resuscitation techniques, novel cell preservation strategies, modulation of response to lethal insults, therapeutic hypothermia, hemorrhage control, and development of new treatments for sepsis. This research is funded by large federal grants by the National Institutes of Health as well as by the US Department of Defense. He has published nearly 200 manuscripts and book chapters and is the holder of 6 patents. He has won numerous awards for excellence in teaching and research, and serves on the editorial boards of nearly all of the leading surgical, trauma and critical care journals.

Frederic C. Blow, PhD
Professor of Psychiatry
Director, Addiction Center
Adjunct Associate Professor of Psychology
University of Michigan Medical School

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Dr. Blow joined the University of Michigan faculty in 1986 and is a Professor and Director of the Addiction Center in the Department of Psychiatry, and a Senior Research Scientist at the Department of Veterans Affairs Center for Clinical Management Research at the Ann Arbor VA Healthcare System. Additionally, since 2001 he has been the first National Huss Family/Hazelden Betty Ford Foundation Endowed Research Chair on Substance Abuse in Older Adults at the Butler Center for Research at the Hazelden Betty Ford Foundation. He is a researcher and educator in the field of alcohol and substance use screening, interventions, and treatments. His areas of research expertise include alcohol and drug brief interventions in healthcare settings, eHealth interventions, substance abuse prevention, substance abuse screening and diagnosis for older adults, serious mental illness and concurrent substance abuse, mental health services research, and implementation of evidence-based substance abuse and mental health practices. Dr. Blow has been the principal investigator on numerous U.S. federal, state and foundation grants and has published over 350 papers and book chapters, and several books. The large body of his work has been directed to providing the research base and training scholars and clinicians alike. He has received a number of awards in recognition of his accomplishments including the Annual Clinical and Health Services Research Award and the League of Research Excellence Award, both from the University of Michigan Medical School, and the Distinguished Mentor Award from the University of Michigan Center for Health Research.

Amy Bohnert, PhD, MHS
Associate Professor of Psychiatry
Associate Director, Opioid Use Case of the UM Precision Health Initiative

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Dr. Bohnert received her MHS and PhD at Johns Hopkins University. Her research focuses on prescription drug overdose and interventions regarding substance use and related disorders, including brief motivational interventions to improve safe use of opioids among VA patients and to reduce overdose risk among individuals in residential addictions treatment. She has led a number of projects related to overdose and prescription drug safety, many aimed at improving care occurring in substance use disorder treatment settings. She is also working on analyses of medical records data linked to mortality data in order to improve prescribing practices. She has provided scientific guidance to the Governor's Prescription Drug and Opioid Abuse Task Force (MI) and is a member of the core expert group that provided guidance to the CDC in developing its opioid prescribing guidelines for chronic pain. She co-directs the Mental Health Innovation, Services and Outcomes Program (MHISO) within the U-M Department of Psychiatry.

Chad Brummett, MD
Associate Professor, Anesthesiology
Director, Anesthesia Clinical Research
Director, Division of Pain Research

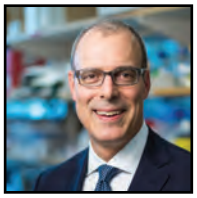
Email: cbrummet@med.umich.edu

Dr. Brummett attended medical school at Indiana University and completed residency and fellowship at U-M and Johns Hopkins Hospital, respectively. His interests include predictors of chronic post-surgical pain as well as failure to derive benefit from interventions and surgeries done primarily for pain. In particular, Dr. Brummett is interested in the impact of a fibromyalgia-like or centralized pain phenotype on surgical outcomes and prediction of response to interventions for chronic pain (e.g. Epidural steroid and facet injections). He also leads an institution-wide initiative to create a biorepository for research of genetic factors associated with the development of disease and response to treatment. In addition, Dr. Brummett was the first to describe the use of peripheral perineural dexmedetomidine, and his early research focused on the efficacy, safety and mechanisms of dexmedetomidine added to local anesthetics for peripheral nerve blocks. He has since translated that work to humans.

Arul Chinnaiyan, MD, PhD
Director, Michigan Center for Translational Pathology
S.P. Hicks Endowed Professor of Pathology
Professor of Urology

Email: arul@umich.edu

Dr. Chinnaiyan received his undergraduate and graduate training at the University of Michigan. As Director of the Michigan Center for Translational Pathology (MCTP), he leads a multi-disciplinary team of investigators focused on translating "-Omic" technologies to patient care in terms of biomarkers and novel therapeutics. Dr. Chinnaiyan's laboratory is focused on using functional genomic, proteomic, metabolomic and bioinformatics approaches to dissect and understand cancer biology as well as discover biomarkers. He and his collaborators have characterized a number of biomarkers of prostate cancer including AMACR, EZH2, hespin and sarcosine. His laboratory identified recurrent gene fusions of TMPRSS2 to ETS family transcription factors in prostate cancer, potentially redefining the molecular basis of prostate cancer as well as other common epithelial cancers. His laboratory developed the popular cancer profiling bioinformatics resource called Oncomine. He has co-authored over 450 manuscripts and has been designated an A. Alfred Taubman Medical Research Institute Scholar, is an elected member of the American Academy of Arts and Sciences (AAAS), the National Academy of Medicine, the Association of American Physicians (AAP), the American Society for Clinical Investigation (ASCI) the National Academy of Inventors (NAI). He serves on the Board of Scientific Advisors for the National Cancer Institute.



Eric R. Fearon, MD, PhD
Chief, Division of Genetic Medicine
Emanuel N. Maisel Professor of Oncology
Director, University of Michigan
Rogel Cancer Center
Professor of Internal Medicine, Pathology, and Human Genetics
University of Michigan Medical School

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Dr. Fearon received his medical and doctorate degrees from Johns Hopkins University before joining U-M in 1995 as Associate Director for Basic Science Research at the Rogel Cancer Center. His role within the Center expanded in 2005 to Deputy Director, and he was named Director in 2016. The Center is currently ranked 15th in the nation (and number one in Michigan) for cancer care by US News and World Report and is among just 49 cancer programs in the United States designated by the National Cancer Institute as a Comprehensive Cancer Center. Dr. Fearon has pursed research in the cancer genetics field, particularly investigations of selected gene defects that underlie colon and rectal tumor development and progression to advanced stages. The author of more than 135 peer-reviewed research manuscripts and more than 60 review/editorial articles and book chapters, Dr. Fearon has served on the editorial boards of various journals in the cancer biology and human genetics fields and currently is an editorial board member or editor for a number of journals, including *The Journal of Biological Chemistry*, *Current Biology*, *Journal of Clinical Investigation*, *Gastroenterology* and *Molecular Cancer Research*. In addition, he has served as a member or chair of various National Institutes of Health and National Cancer Institute advisory groups and grant review committees, including the Panel to Investigate the NIH Investment in Gene Therapy, the National Cancer Institute Board of Scientific Advisors, and the NIH Pathology B and Cancer Genetics Study Sections.

MeiLan K. Han, MD, MS
Professor of Pulmonary Medicine, Critical Care
University of Michigan Medical School

Email: mrking@med.umich.edu

Dr. Han received her medical degree from the University of Washington in Seattle, WA. She completed her residency in Internal Medicine and fellowship in Pulmonary and Critical Care Medicine at the University of Michigan. Dr. Han has also completed a Master's Degree program in Biostatistics and Clinical Study Design at the University of Michigan School of Public Health. Dr. Han is co-chair of the University of Michigan COPD Quality Improvement Committee and co-authored the University of Michigan COPD Guidelines. Dr. Han's research has focused on defining phenotypes in COPD using imaging. She is a lead investigator for several NIH sponsored COPD studies. She also serves on the scientific advisory committees for both the COPD Foundation and American Lung Association and serves as a spokesperson for the American Lung Association. She is currently an Associate Editor for the *American Journal of Respiratory and Critical Care Medicine* and serves on the editorial boards for *Thorax*, *Lancet Respiratory Medicine* and the *Journal of the COPD Foundation*.

Joseph C. Kolars, MD
Senior Associate Dean for Education and Global Initiatives
Josiah Macy, Jr., Professor of Health Professions Education
University of Michigan Medical School

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Dr. Kolars obtained his MD degree in 1982 from the University of Minnesota Medical School, pursued internal medicine training in Minneapolis, and completed his post-graduate training gastroenterology at the University of Michigan in 1989. After serving as Associate Chair for Medicine and Residency Program Director, Dr. Kolars left the University of Michigan to establish a western based health care system in China in conjunction with Shanghai Second Medical University. He lived with his family in Shanghai for three years. In 1999, he joined the faculty at Mayo Clinic in Rochester, Minnesota and served as internal medicine residency program director for 5 years. In June of 2009, he moved to the University of Michigan where he oversees the Associate Deans responsible for the education programs as well as global health initiatives for the medical school. Between 2007-2011, he worked closely with the Bill and Melinda Gates Foundation to partner medical schools in the U.S. with those in sub-Saharan Africa. He currently serves as co-director for the Michigan Medicine – Peking University Health Science Center Joint Institute for Clinical and Translational Research. Current interests in medical education focus on innovations and the transformation of learning systems to more explicitly align with better health.

Steven Kunkel, PhD
Senior Associate Dean for Research
Endowed Professor of Pathology
University of Michigan Medical School

Email: slkunkel@umich.edu

Dr. Kunkel provides direction for the school's research mission, including setting goals for developing a major global presence for the Medical School's research enterprise. He received his PhD from the University of Kansas in microbiology and served his postdoctoral fellowship at the University of Connecticut Health Center. He joined the University of Michigan Medical School faculty in 1980. Dr. Kunkel's areas of research have centered on assessing molecular mechanisms of lung inflammation by investigating cytokine and chemokine directed cell-to-cell communication circuits. His studies in cytokine and chemokine biology are internationally recognized and have provided a clearer understanding of how these proteins participate in the initiation, maintenance, and resolution of acute and chronic lung. His research group has provided evidence for specific cytokine phenotypes that dictate the progression of particular chronic diseases. Dr. Kunkel has co-authored more than 600 peer-reviewed manuscripts, contributed more than 60 chapters to different books in his field, served as the editor for four books, presented 150-plus lectures as a visiting professor/lecturer in the past 10 years, and maintained continuous funding of multiple National Institute of Health grants for a number of years, including the principal investigator of a program project to study lung inflammation. He is the recipient of a previous NIH MERIT Award, served on National Institute of Health peer review study sections, organized numerous international conferences on inflammation, and is an associate editor for various professional scientific journals. He is the present co-chair of the Board of Scientific Counselors for the NIAID-NIH.

Subramaniam Pennathur, MD
Norman Radin Professor
Chief, Division of Nephrology
Director, Michigan Kidney Translational Research Center
Departments of Internal Medicine & Molecular and Integrative Physiology
University of Michigan Medical School

Email: spennath@umich.edu

Dr. Subramaniam Pennathur completed his clinical training in internal medicine, endocrinology and nephrology at Washington University, Saint Louis and research fellowships at Massachusetts General Hospital, (Harvard University), Washington University, Saint Louis and the University of Washington, Seattle. He is currently the Norman Radin Professor and Chief, Division of Nephrology, Director, O'Brien Kidney Translational Research Center, Departments of Medicine and Molecular and Integrative Physiology, University of Michigan. His laboratory focuses on understanding molecular mechanisms of diabetic kidney disease, mechanisms of atherosclerosis, translational research and biomarker discovery. His work is funded by the National Institutes of Health, American Diabetes Association and the Juvenile Diabetes Research Foundation. The central theme of Dr. Pennathur's research has focused on the applications of biological mass spectrometry in disease pathogenesis. His laboratory has utilized mass spectrometry to identify key protein and metabolite alterations in disease states and tested the hypothesis whether these alterations predict complications in animal models and humans. Dr. Pennathur's strategy has been to develop analytical techniques in animal models and validate these markers in humans and then interrogating the animal model for biological pathway relevance. Recent extension of this work has included targeted as well as unbiased metabolomics and proteomic profiling.

J. Scott Roberts, PhD
Professor of Health Behavior & Health Education
Director, Public Health Genetics Program
U-M School of Public Health

A clinical psychologist by training, Dr. Roberts conducts research on the psychosocial implications of genetic testing for adult-onset diseases. He has served since 2001 as Co-Principal Investigator on the NIH-funded REVEAL Study (Risk Evaluation and Education for Alzheimer's Disease), a series of randomized clinical trials examining the impact of genetic susceptibility testing for people at risk for AD. Dr. Roberts has published numerous articles that address participants' motivations and interests in genetic testing, the psychological impact of providing risk disclosure, and health behavior changes prompted by risk assessment. He has also examined ethical and practical issues involved in the returning of research results to individuals enrolled in cancer genetics studies.

Marschall S. Runge, MD, PhD
Executive Vice President for Medical Affairs
Dean, University of Michigan Medical School
CEO, Michigan Medicine

The University of Michigan Board of Regents appointed Marschall S. Runge Executive Vice President for Medical Affairs and CEO of Michigan Medicine effective March 2015 and Dean of the Medical School effective January 2016. Before coming to Michigan, Dr. Runge was executive dean for the University of North Carolina (UNC) School of Medicine, the Charles Addison and Elizabeth Ann Sanders Distinguished Professor of Medicine at UNC-Chapel Hill (UNC-CH), chair of the UNC-CH Department of Medicine, and principal investigator and director of the NIH-funded North Carolina Translational and Clinical Sciences (NC TraCS) Institute, one of 55 medical research institutions working together as a national consortium to improve the way biomedical research is conducted across the country.

An honors graduate of Vanderbilt University with a B.A. in Biology and a Ph.D. in Molecular Biology, Dr. Runge earned his M.D. from the Johns Hopkins School of Medicine, where he was an intern and resident in internal medicine. He then completed a cardiology fellowship at Harvard's Massachusetts General Hospital and was a faculty member at Harvard prior to subsequent career moves. Dr. Runge has been a physician-scientist for his entire career, combining basic and translational research with the care of patients with cardiovascular diseases and education. He is the author of over 200 publications in the field and holds five patents for novel approaches in healthcare.

Srijan Sen, MD, PhD
Associate Chair for Research and Research Faculty Development
Frances and Kenneth Eisenberg Professor of Depression and Neurosciences
University of Michigan Medical School

Dr. Sen received his MD and PhD from the University of Michigan and completed residency at Yale. His research focuses on depression, specifically on interactions between genes and the environment and their effect on stress, anxiety, and depression. He also has an interest in medical education and leads a large multi-institution study that uses medical internship as a model of stress.

Mark S. Schlissel, MD, PhD
President
University of Michigan

Dr. Schlissel is the 14th president of the University of Michigan and the first physician-scientist to lead the institution. Since beginning as president in 2014, he has launched initiatives including Academic Innovation; Biosciences; Diversity, Equity and Inclusion; Poverty Solutions; and Precision Health. As part of his commitment to college affordability, President Schlissel in June 2017 announced the Go Blue Guarantee, a new financial aid program that provides up to four years of free undergraduate tuition to in-state students from families in Michigan making $65,000 or less. U-M is perennially the nation's top public university in research productivity and is consistently ranked as the No. 1 or among the top public universities in the nation. A graduate of Princeton University, he earned both MD and PhD degrees at the Johns Hopkins University School of Medicine before completing residency training in internal medicine at Hopkins Hospital and conducting postdoctoral research as a Bristol-Myers Cancer Research Fellow under David Baltimore at the Massachusetts Institute of Technology's Whitehead Institute. His research has focused on the developmental biology of B lymphocytes, the cell type in the immune system that secretes antibodies. His work has contributed to a detailed understanding of genetic factors involved in the production of antibodies and how mistakes in that process can lead to leukemia and lymphoma. He is the author or coauthor of more than 100 scientific papers and has trained 21 successful doctoral candidates in his lab.

Nationally, he has served as member and chair of the Immunobiology Study Section at the National Institutes of Health and on the Howard Hughes Medical Institute's Scientific Review Board. President Schlissel was elected to the American Society of Clinical Investigators in 1998 and the American Association of Physicians in 2013.

He has been a member of the American Association of Immunologists since 1992. He was elected as a Fellow of the American Association for the Advancement of Science in 2013 and as Fellow of the American Academy of Arts & Sciences in 2015. He has helped organize major international scientific meetings and is a frequent seminar speaker at universities throughout the United States.

Anne Schott, MD
Clinical Professor of Medicine
Associate Director of Clinical Research
Rogel Cancer Center
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Dr. Schott is a Clinical Professor of Medicine and is the Associate Director of Clinical Research for the Rogel Cancer Center. She is an expert in the field of breast cancer, and frequently gives lectures and publishes about breast cancer treatment. She is also Deputy Chair of SWOG, a national clinical trials organization funded by the National Cancer Institute, which runs clinical trials for all types of cancer. Her research is focused on the development of new treatments for breast cancer, and the testing of these treatments in clinical trials.

Kathleen Stringer, PharmD, FCCP
Albert B. Prescott Professor of Pharmacy
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Dr. Stringer is a Professor of Clinical and Translational Pharmacy and Internal Medicine, Pulmonary and Critical Care Medicine and the Director, the Nuclear Magnetic Resonance (NMR) Metabolomics Laboratory at the University of Michigan. She was a faculty member at the University of Colorado School of Pharmacy before joining the faculty of the University of Michigan in 2007. She received her PharmD degree from the University of Michigan, completed a clinical residency at the University of Illinois, Chicago and a post-doctoral fellowship at the State University of New York at Buffalo. Dr. Stringer's translational research program utilizes experimental and clinical models to tackle therapeutic problems associated with inflammatory pulmonary diseases including chronic obstructive pulmonary disease and critical illnesses like sepsis. She is pioneering new techniques in metabolomics, in particular, methods that employ NMR. She has incorporated the use of this science in her work which is supported by the National Institutes of Health (NIH). Dr. Stringer is a member of the American Thoracic Society and serves as a mentor on the Department of Pulmonary and Critical Care Medicine's NIH-funded T32 Multidisciplinary Training Program in Lung Disease.

Thomas Wang, MD, PhD
Professor, Internal Medicine, Biomedical Engineering, & Mechanical Engineering
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Dr. Wang is PI in the NIH-funded Michigan Barrett's Esophagus Translational Research Network (BETRNet) and Consortium in Imaging and Biomarkers (CIB). He is a board certified gastroenterologist with over 30 years of experience in developing novel optical imaging instruments and molecular probes. Dr. Wang has pioneered the development of wide area fluorescence imaging, the dual axes confocal endomicroscope, and clinical use of fluorescent-labeled peptides for early detection of cancer in the digestive tract. In addition, he is experienced at validating novel imaging platforms, and applies his broad training to significantly accelerate the bench to bedside process. Dr. Wang attended Harvard Medical School where he received his MD in 1996. He earned a PhD in Medical Engineering and Medical Physics at the Massachusetts Institute of Technology in 1998. Dr. Wang has published over 75 original peer-reviewed papers on imaging and advanced technologies, including molecular imaging, biomarker identification and validation, targeted imaging agents, and early detection of cancer in the digestive tract.

Poster Abstracts

海报内容摘要

Poster Abstracts

While the official poster session will take place Tuesday, Oct.16 from 3:45 to 5 p.m. in the Biomedical Science Research Building (BSRB) atrium, posters will remain available for viewing throughout Tuesday and Wednesday.

CANCER #1

Epigenetic Upregulation of the DNA Damage Response in Mutant IDH1 Gliomas

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3. University of Miami Health System

PURPOSE: Glioma patients whose tumors carry a mutation in the Isocitrate Dehydrogenase 1 (IDH1-R132H) gene, exhibit increased survival. The glioma subtype which we modelled harbors IDH1-R132H, tumor protein 53 (TP53) and alpha–thalassemia/mental retardation syndrome X-linked (ATRX) loss. The impact of IDH1-R132H on genomic stability, DNA damage response (DDR) and DNA repair in this molecular glioma subtype is unknown.

METHODS: We developed a mutant IDH1 mouse glioma model harboring IDH1-R132H, TP53 and ATRX knockdown using the Sleeping Beauty (SB) Transposase system. NRAS, shP53 and shATRX plasmids were delivered in the lateral ventricle of neonatal mice with or without IDH1-R132H. Tumors were used to generate neurospheres (NS) for in vitro analysis; moribund animals were perfused and analyzed using immunocytochemistry to assess neural precursor cells' differentiation markers and enzymes involved in DNA damage response (DDR) and DNA repair. We performed ChIP-seq at the whole genome level to analyze epigenetic regulation of gene expression and RNA-seq to assess the impact of mIDH1 of the tumor transcriptome.

RESULTS: We discovered that IDH1-R132H expression in the genetic context of ATRX and TP53 inactivation: (i) increases median survival (MS), (ii) enhances DDR activity via epigenetic upregulation of Ataxiatelangiectasia mutated (ATM) signaling, and (iii) elicits tumor radioresistance. Pharmacological inhibition of ATM or checkpoint kinase 1 and 2 (CHK1/2), two essential kinases in the DDR pathways, restored tumor radiosensitivity.

CONCLUSIONS: We created genetically engineered mice expressing IDH1-R132H in combination with TP53 and ATRX knockdown which displayed phenotypic features of mutant IDH1 gliomas exhibiting increased MS. The genetically engineered mIDH1 glioma model enabled us to determine the impact of glioma-specific genetic lesions on DDR ad DNA repair mechanisms. Translation of these findings to mIDH1 glioma patients could significantly improve the therapeutic efficacy of radiotherapy, and have a major impact on patient survival.

CANCER #2

Self-organization of Brain Tumors: Oncostreams Determine Growth, Invasion, and Malignity of Brain Tumors

Lowenstein PR (1, 2), Comba A (1), Zamler D (1), Argento A (1), Nunez-Aguilera F (1), Kahana A (3), Kish P (3), Dunn P (1), Motsch S (4), Castro MG (1, 2)

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2. Department of Cell and Developmental Biology, University of Michigan Medical School
3. W.K. Kellogg Eye Center, University of Michigan
4. School of Mathematical and Statistical Sciences, Arizona State University

ABSTRACT: Biological self-organization is when a process or a biological multicellular structure forms at the macroscopic level as a result of interactions among lower-level components, i.e., individual cells. The role that stereotypical structures may have on tumor growth is not well understood.

From the study of both rodent and human gliomas we determined the existence of multicellular structures which we named oncostreams, comprised of elongated cells 5-20 cells wide and of variable length. Oncostreams express proteins typical of brain tumors, i.e., GFAP, nestin, twist, MMP2, retinoblastoma, olig2, amongst others. We explored the function of oncostreams utilizing cell biological, molecular, and mathematical modeling techniques. Our data demonstrated that oncostreams mediate invasion, as they form fingers of parallel elongated cells that push into the surrounding normal brain, and serve as highways for the movement of glioma cells throughout the brain. Injection of slowly moving human glioma stem cells into rapidly streaming rodent glioma tumors results in the alignment of the human glioma cells to the oncostreams, and their distribution throughout the tumor along these structures. Oncostreams may also limit immune cells' entry into gliomas.

To test the hypothesis that oncostreams are formed solely from interactions between individual glioma cells, we built agent-based mathematical models. These allowed us to discover that only elongated cells form structures resembling oncostreams. Circular cells never do so. The length:width ratio of the elongated oncostream-forming cells is not significantly different from the ratio measured in vivo.

To understand whether oncostreams differ molecularly from surrounding glioma cells, we dissected oncostreams and surrounding glioma tissue using laser scanning microdissection, followed by RNA-Seq and bioinformatics. The set of gene expression patterns differs significantly between the two areas, thus enabling us to identify novel enriched signaling pathways operating within the oncostreams. Network analysis identified fyn and STAT-1 as highly connected nodes. Data from deletion studies demonstrated that fyn appears to play a role in oncostream formation and malignant tumors' phenotype.

In conclusion, we demonstrate that oncostreams are a novel cancer structure with individual molecular makeup and function, which play a critical role in determining the phenotype and behavior of gliomas. We hypothesize that by disrupting these oncostreams. using gene therapy technologies, we will be able to develop novel treatments for this devastating cancer.

CANCER #3

Metabolic Lipidomic Profiling Identifies Phospholipase A2 as a Novel Therapeutic Target that Significantly Reduces Tumor Growth in Head and Neck Cancer: An Opportunity for Collaboration

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2. Department of Pathology and Michigan Regional Metabolics Resource Core, University of Michigan Medical School
3. Department of Bioinformatics and Michigan Regional Metabolics Resource Core, University of Michigan Medical School

BACKGROUND: There are about 74,500 and 60,000 HNSCC cases diagnosed annually in China and the US respectively. The five-year survival rates of high risk HNSCC have not significantly changed in over three decades with a median survival of less than a year. It is therefore imperative to find better

therapies for patients with advanced disease and one of the best routes is through identification of novel yet tumor-specific biomarkers from which the drugs can be designed. Since lipids play an important role in tumor development and progression of cancer and can be very specifically overproduced in several tumors, lipid metabolic profiling of HNSCC is a unique untapped mechanism to identify novel therapeutic targets for HNSCC. Additionally, this will give information about global and regional differences in the lipid profile of HNSCC leading to personalized biomarker identification.

METHODS: Mass spectrometry (LC/MS), based shotgun untargeted global lipidomic profiling will be used to explore the lipid signatures of both pre and post therapy HNSCC patients. Approximately 50-60 patients will be recruited from both US and China. Lipid profiling of tumors and blood plasma samples will be evaluated by short gun lipidomics to identify novel biomarkers.

RESULTS: Our preliminary data of unsupervised principal component analysis of the lipid signature from US patients showed a very distinct and clear separation between the benign and cancer tissues. A total of 576 lipids were identified of which 322 were significantly different between benign and cancer tissues ($p<0.05$). Evaluation of the top 40 significantly expressed lipids showed up regulation of free fatty acids (24:1, 24:2,24:3 and 22;3), phospholipids such as lysophosphotidyl choline (LPC) in cancer tissues compared to benign tissues whereas glycero-lipids such as triglycerides (TG) were down regulated in cancer tissues. Since upregulation of LPC is catalyzed by PLA2, its activity was measured both in tumor samples as well as in HNSCC cell lines. Tumor samples showed 3.0 fold higher expression levels of cPLA2 compared to benign samples ($p<0.01$) whereas cell lines showed only 2.5 fold upregulation compared to control fibroblast cell lines ($p<0.01$). Treatment of HNSCC xenogaft with ATK resulted in significant (>90%) reduction in tumor volume compared to vehicle treatment groups ($p<0.01$). Animal weight and organs all showed no signs of toxicity with treatment.

CONCLUSION: Preliminary lipid profiling of HNSCC patient tumors from US identified up regulation of FFA and LPC indicating PLA2 as a potential therapeutic target for HNSCC. Blocking of PLA2 activity using ATK resulted in significant growth reduction of HNSCC xenografts without any measured toxicity. This is a very exciting, novel, and highly translatable treatment option for HNSCC with high clinical potential. Further evaluation of the lipid profiles of larger cohort of HNSCC patients from both US and China will result in the development of novel unique biomarker panel. Furthermore, it will shed light on how regional and dietary differences influence the lipid profiling of HNSCC patients.

CANCER #4

Cancer Stem Cell Vaccine Synergizes with Anti-PD-L1 in Reducing Local Tumor Relapse and Prolonging Survival in the Adjuvant Setting

Jing Zhang(1), Yangyang Hu(1), Alfred E. Chang(1), Elaine Hurt(2), John Owen(1), Jeffrey S. Moyer(1), Mark E.P. Prince(1), Joel Whitfield(1), Max S. Wicha(1), Qiao Li(1)

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BACKGROUND: The therapeutic efficacy of standard surgical resection for solid malignancies is limited by both local and distant recurrence. The existence of micro-metastasis at the time of tumor resection represents a great therapeutic challenge. There is increasing evidence that many cancers are driven and maintained by a subpopulation of cells displaying stem-like properties. Targeting cancer stem cells (CSCs) may thus increase the therapeutic efficacy of current cancer treatment.

METHODS: We previously described a strategy to target CSCs using CSC-dendritic cell (DC) vaccination. However, the efficacy of CSC targeted therapeutics may be greatest when they are deployed in the adjuvant setting. In this study, two mouse models were utilized: SCC7 subcutaneous (s.c.) tumors, and D5 melanoma model.

RESULTS: Established s.c. SCC7 tumors were surgically removed from mice followed by $ALDH^{high}$ SCC7 CSC-DC vaccine treatment, which significantly reduced local tumor relapse and prolonged animal survival. This effect was significantly augmented by simultaneous administration of anti-PD-L1 mAb. In the minimal disease setting of D5, $ALDH^{high}$ CSC–DC vaccination significantly inhibited tumor growth, reduced spontaneous lung metastases resulting in increased survival. CCR10 and its ligands were down-regulated on $ALDH^{high}$ D5 CSCs and in lung tissues respectively in animals subjected to $ALDH^{high}$ D5

CSC–DC vaccination. Down-regulation of CCR10 by siRNA significantly blocked tumor cell migration in vitro and metastasis in vivo. T cells harvested from ALDHhigh D5 CSC–DC vaccinated animals selectively killed ALDH^{high} D5 CSCs. There was also evidence of humoral immunological targeting of CSCs. As a result, CSC-DC vaccination significantly decreased the percentage of ALDH^{high} cells in residual tumors.

CONCLUSIONS: When used in an adjuvant setting, ALDH^{high} CSC–DC vaccines effectively inhibit local tumor recurrence, reduce spontaneous lung metastasis, and prolong animal survival, compared with traditional DC vaccines and simultaneous PD-L1 blockade can significantly enhance this effect.

FUNDING: The Elsa U. Pardee Foundation, the Gillson Longenbaugh Foundation and the NCI research grant 1R-35CA197585 (M.S. Wicha).

CANCER #5

Adoptively Transferred B Cells Directly Kill Tumor Cells via the CXCR4/CXCL12 and Perforin Pathways

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2. The No. 1 People's Hospital of Hefei, China

BACKGROUND: The role played by B cells in cancer immunology is complex and controversial. The observation made by our lab that activated B cells alone can mediate tumor regression in the adoptive immunotherapy of solid tumors is innovative (JI 2009; CCR 2011; JSO 2012; EJI 2015). We previously reported that antitumor B cells directly kill tumor cells via the Fas/FasL pathway and are regulated by IL-10. In this study, we defined additional mechanisms involved in B cell antitumor immunity.

METHODS: We examined the pathways contributing to B cell-mediated antitumor immunity, including the impact of IL-2, the CXCR4/CXCL12 pathway and perforin in mediating tumor regression after the adoptive transfer of B effector cells.

RESULTS: IL-2 significantly augmented the efficacy of adoptively transferred tumor-draining lymph node (TDLN) B cells which express IL-2R. Culture supernatant of purified B splenocytes harvested from the mice that received adoptive transfer of 4T1 TDLN B cells plus IL-2 administration produced larger amounts of IgG which bound to 4T1, resulting in 4T1 lysis. Transwell experiments demonstrated the chemotraction of CXCR4-expressing 4T1 TDLN B cells towards CXCL12-producing 4T1 cells. Blockade of CXCR4 using a CXCR4-specific inhibitor, AMD3100, significantly reduced the killing of 4T1 tumor cells by 4T1 TDLN B cells. Blockade of FasL and CXCR4 concurrently inhibited B cell-mediated direct killing of tumor cells in an additive manner. Additional transwell experiments showed that effector B cells could directly kill tumor cells in cell-cell contact via the Fas/FasL and CXCR4/CXCL12 pathways as well as perforin.

CONCLUSIONS: These findings underscore the diversity of function by which B cells can play an important role in the host immune response to tumor, and clearly indicated that transferred effector B cells can act independently of T cells in causing tumor destruction in adoptive immunotherapy.

FUNDING: The Gillson Longenbaugh Foundation, National Natural Science Foundation of China (30971112), and The First Plan of Science and Technology Program of Hefei City, China.

CANCER #6

Imaging Biomarkers for Staging and Assessing Response to Therapy in Multiple Myeloma

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PURPOSE: The purpose of this study is to evaluate the performance of the MRI biomarker using an independent test set of prospective MRI cases for treatment response assessment of multiple myeloma (MM).

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METHOD: A 3D dynamic intensity entropy transformation (DIET) method was developed to characterize MM infiltration in bone marrow. DIET transforms the MR T1-weighted (T1W) signals in a vertebral body voxel-by-voxel to a quantitative entropy enhancement value (qEEV). qEEV is calculated as a posteriori entropy of intensity at the voxel normalized by the median a posteriori entropy of intensity in the adjacent intervertebral discs. The reference standard of treatment response was determined by clinical outcomes using the international myeloma working group (IMWG) uniform response criteria.

With IRB approval, we prospectively enrolled 19 patients diagnosed with MM and collected pre- and post-treatment spinal MR scans at the baseline (the first scan since enrollment) and follow up with about 3-month interval. The MRI data were acquired with GE or Philips 3.0T scanners. We applied DIET method to the collected 19 cases to monitor MM progression or regression. The clinical outcome (>6-month after baseline) was used as the reference standard of MM progression for each patient. The performance of quantitative qEEV-based response (qERI) as a radiomic biomarker for the discrimination of responders and nonresponders was evaluated by receiver operating characteristic (ROC) curve analysis.

RESULTS: Of the 19 prospective patients, 13 and 6 were clinically diagnosed as responders and nonresponders, respectively. Using at a decision threshold chosen by the previous retrospective study, the qERI correctly identified 12 responders (92.3% sensitivity) and 4 nonresponders (66.7% specificity). The agreement between the DIET method and the clinical outcome reached 0.84 (16 of 19) with a kappa value of 0.62. With the ROC analysis, the AUC achieved 0.80.

CONCLUSION: The study demonstrated the feasibility of quantitative response index to differentiate responder and nonresponder patients and had substantial agreement with clinical outcomes, which indicated that this quantitative measure has the potential to be an image biomarker to assess MM treatment response.

CANCER #7

Development and Applications of the Community-based Ontology of Host-Microbiome Interactions (OHMI) for Standardized Data and Knowledge Representation and Analysis of Host-Microbiome Interactions Under Different Conditions

Yongqun He(1), Haihe Wang(1,2), Hong Yu(1,3), Jie Zheng(4), Daniel P. Beiting(5), Anna Maria Masci(6), Timothy Putman(7), Barry Smith(8), Alexander V. Alekseyenko(9), Jihad S. Obeid(9)

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5. University of Pennsylvania School of Veterinary Medicine, Philadelphia
6. Duke University School of Medicine, Durham
7. Oregon Health and Science University, Portland
8. University at Buffalo, Buffalo
9. Medical University of South Carolina, Charleston

BACKGROUND: Host-microbiome interactions (HMI) are critical determinants of host development and defense. The large volume of HMI data being generated poses a significant challenge to the research community. Reproducibility of experiments depends on consistent procedures employed across different settings. Although there are existing standards for representing microbial organisms, the terminology of the interactions between microbiomes and hosts along with associated biological processes has not been harmonized, preventing integration and systems-level analysis of HMI data produced by different laboratories and institutions.

METHODS: To address these challenges, we developed and applied a community-based Ontology of Host-Microbiome Interactions (OHMI; https://github.com/OHMI-ontology/OHMI) through a multi-institutional collaboration. OHMI was developed by following the Open Biomedical Ontologies (OBO) Foundry principles (e.g., openness and collaboration). Use cases were identified and studied.

RESULTS: OHMI logically represents microbiome, host species and associated taxonomy hierarchy, host anatomic entities, HMI conditions, protocols, resulting data and analyses. OHMI leverages established ontologies. Different OHMI use cases are examined, including rheumatic diseases (e.g., rheumatic arthritis, ankylosing spondylitis), which are associated with microbiome patterns in different human anatomic locations. From over 100 peer-reviewed publications, we identified 171 bacteria and fungus from gut, oral, skin, and airway that are associated with 6 rheumatic diseases. These results were represented in OHMI. Analysis through this representation identified new scientific insights. Furthermore, we used OHMI to model different HMI experimental metadata types and applied it to experimental studies. Other use cases include those related to prokaryotic 16S rRNA sequence analysis, antibiotics effects on microbiome, gut microbiome influences on human diseases (e.g., obesity, diabetes, and cancer), and HMI molecular mechanism modeling.

CONCLUSIONS: Our work suggests that OHMI permits improved sharing of data, knowledge, analyses and results in translational HMI studies.

FUNDING GRANTS: UL1TR002240, UL1TR001450, UL1TR001412, R01LM012517, U54CA210962, P50AR070591, UL1TR001450, and MUSC College of Medicine Enhancing Team Science (COMETS) award.

CARDIOVASCULAR

#8

BAF60a Deficiency in Smooth Muscle Cell Attenuates Angiotensin II Induced Abdominal Aortic Aneurysm

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BACKGROUND: Abdominal aortic aneurysm (AAA) is a chronic disease and has high mortality rate when ruptured. As a major component of artery wall, vascular smooth muscle cells (vsmc) play an important role in the pathogenesis of aaa. Baf60a serves as a key factor that links the swi/snf chromatin remodeling complex to transcription factors. It has been reported that baf60a plays a pivotal role in maintaining metabolism homeostasis. In smooth muscle cells, baf60a stimulates the transcription of clock genes and inhibits cell proliferation and migration. However, it remains unclear whether baf60a in smooth muscle cells has a potential effect in the development of aaa.

METHODS & RESULTS: The AAA model was induced in BAF60af/f-smMHC-CreERT2 and BAF60af/f mice by PCSK9D377Y.AAV injection and Angiotensin II (Ang II) infusion (1500ng/kg/day for 4 weeks). Smooth muscle cell-specific BAF60a deletion (SMC-BAF60a-KO) significantly protected mice from Ang II infusion-induced AAA, with decreased incidence, rupture rate and maximum aortic diameter. BAF60a knock out in SMC alleviated the degradation of elastin fibers and decreased the expression of matrix metallopeptidase 9 (MMP9), which is a known factor associated with AAA in patients. We also found that BAF60a overexpression in cultured VSMC elevated MMP9 expression and activity. Through RNA sequencing and microarray analysis, we found that BAF60a knockout in SMC affects genes involve in vascular smooth muscle contraction, inflammation and focal adhesion.

CONCLUSIONS: These results revealed an important role of BAF60a in the pathogenesis of AAA through regulating MMP9 expression and vascular wall inflammation. It suggests that interfering BAF60a or its downstream pathways may be a potential therapeutic strategy to treat AAA.

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CARDIOVASCULAR
#9

Detect the Role of SMAD3 Gene Mutation in Thoracic Aortic Aneurysm Using Human Induced Pluripotent Stem Cells

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University of Michigan Department of Cardiac Surgery

INTRODUCTION: Smad3 protein is a key mediator of TGFβ signaling pathway. SMAD3 gene mutations could cause an autosomal dominant aneurysms–osteoarthritis syndrome(AOS) that characterized by arterial aneurysms and early-onset osteoarthritis. High occurrence rate of thoracic aortic aneurysm(TAA) with the aortic vascular medial degradation have been identified in the AOS patients. Knock out SMAD3 in mice could also cause TAA. These indicate a strong linkage between SMAD3 mutation and TAA development. However, the mechanism for SMAD3 mutation causing TAA is still unclear.

HYPOTHESIS: We hypothesis that SMAD3 mutation could affect vascular smooth muscle cells (VSMCs) differentiation and extracellular matrix(ECM) deposition. The resulting abnormalities in the VSMCs may cause structure and function deficiency in aortic wall and lead to TAA development.

METHOD: Human induce induced pluripotent stem (iPS) cells were generate from Peripheral blood mononuclear cells and smad3 gene mutation in an iPS cell line from a healthy individual without TAA using CRISPR-Cas9 system. The WT and modified cell lines were differentiated into neural crest stem cell(NCSC)-derived VSMCs in vitro, which representing embryo origin of VSMCs located in aorta root and ascending aorta in vivo. Differentiation, contraction, and ECM synthesis of the differentiated VSMCs were analysis.

RESULTS & CONCLUSION: A homozygote with SMAD3 frameshift mutation was created. It contained a 7-base-pair deletion in the exon 5 of SMAD3 gene and Smad3 protein were removed in this homozygote according to qPCR and Western blot result. Both WT and Smad3 mutation cell line could be induced into NCSC derived SMC successfully. The qRCR and WB result showed that decreased expression of key genes of VSMCs contraction apparatus (ACTA2 and MYH11), as well as ECM components (elastin, collagen type III) in SMAD3 deficiency cell lines, while the MMP9 was up-regulated. These result indicate that SMAD3 mutation may affect VSMCs differentiation, contraction and ECM- construction.

CARDIOVASCULAR
#10

Axon-guidance Molecule SLIT3 Knockout Attenuates Pressure Overload-Induced Left Ventricular Hypertrophy and Failure

Lianghui Gong, Shuyun Wang, Lishen, Yifeng Yang, Dingding Xiong, Ming-Sing Si

University of Michigan Department of Cardiac Surgery

INTRODUCTION: Although axon-guidance molecule SLIT3 is known to regulate many aspects of heart development, its roles in postnatal cardiac remodeling are still unknown. This project aims to explore its function in pathological left ventricular (LV) hypertrophy.

METHODS: Transverse aortic constriction (TAC) was performed in 6-12 weeks old CD1 wild-type (WT) (n=32, 59% female) and SLIT3 knockout (KO) mice (n=28, 42% female). LV function, structure and TAC gradient were assessed by echocardiography. LV hypertrophy was assessed by histology and weight. Hypertrophy-related gene expression of LV free wall was assessed by qRT-PCR. Results at different days (D) and weeks (W) after TAC in two groups are compared by t-test and shown as mean±SEM.

RESULTS: The initial TAC gradient and LV mass in two groups were similar (3D: 43±1.4 vs. 44±1.8mmHg; 4.3±0.2 vs. 3.9±0.2mg/g, p= NS for both), but they increased significantly in WT compared with KO mice (8W: 82±5.7 vs. 45±2.7mmHg; 6.6±0.3 vs. 5±0.3mg/g, both p <0.005). In the first 3 weeks, LV ejection fraction (EF) and fractional shortening (FS) in two groups are normal, but they reduced significantly at 8 weeks in WT compared with KO mice (EF: 48±4% vs. 58±2%; FS: 24±2% vs. 30±1%, both p<0.04). Cardiomyocytes diameter and heart weight to body weight ratio were significantly higher in WT compared with KO mice (3W: 18±0.4 vs. 16±0.3μm, 8W: 6.8±0.4 vs. 5.1±0.2mg/g, both p<0.02). Also, the relative expression of SLIT3, atrial and brain natriuretic peptides (ANP and BNP), myosin heavy chain 7

(MYH7) and connective tissue growth factor (CTGF) were significantly higher in WT compared with KO mice (1W: SLIT3: 1±0.2 vs. 0.1±0.03; ANP: 1±0.08 vs. 0.45±0.1; BNP: 1±0.3 vs. 0.2±0.02; MYH7: 1±0.2 vs. 0.36±0.05; CTGF: 1±0.13 vs. 0.47±0.09, all p<0.02).

CONCLUSIONS: Deficiency of Axon-Guidance molecule SLIT3 Attenuates Pressure Overload-Induced Left Ventricular Hypertrophy and Failure. These data may reveal a new function of SLIT3 and possible therapeutic potential of SLIT3 inhibition to ameliorate LV remodeling in patients with systemic hypertension.

CARDIOVASCULAR #11

In Situ Vascular Reconstruction by Using Heparinized PCL/PLLA Bilayer Nanofibrous Scaffolds in a Rat Model

Longtan Jiang(1), Renato S. Navarro(2), Ouyang Yang(1), Zhiyong Liu(1), Jiawen Luoa(1), Ping Qiua(1), Y. Eugene Chen (1), Peter X. Mab (2), Bo Yang (1)

1. Department of Cardiac Surgery, University of Michigan
2. Macromolecular Science and Engineering Center, University of Michigan

ABSTRACT: Atherosclerotic cardiovascular diseases are the leading death cause in the United States accounting for most of the 610,000 deaths of cardiovascular disease. There is an urgent clinical need for readily-available substitutes for small-diameter blood vessels. Emerging as a new breakthrough technology, biomaterial-driven in situ vascular engineering aims to use cell-free scaffolds that can instruct host cell in recapitulating the 3D-microstructure and microenvironment in malfunctioned vascular sites. We designed biomimetic bilayer nanofibrous scaffolds with tunable diameter and pore size conjugated with heparin through modified poly(l-lactic acid) and electrospinning Poly(ε-Caprolatone). The scaffolds were fabricated with dimensions of 0.9 mm ID, 1.8 mm OD, and 5.0 mm in length, the inner layer is an interconnected porous architecture and able to mimic the extracellular matrix by harboring invading host cells. Its conjugation with anticoagulant heparin prevented thrombosis after implant. The outer layer was not only beneficial for surgery, its slower bio-degradation rate prevented aneurysm, allowing for mature vascular reconstruction. The rat abdominal aortic interposition graft model has been used to check the progress of vascular reconstruction in situ. Longitudinal ultrasound data showed that the implanted scaffolds remain patent and no aneurysm in all rats 3 months post-operation. Histology analysis showed that progressive vascular reconstruction occurred over time, including mature vascular smooth muscle cell infiltration and proliferation in inner layer leading to scaffold remodeling. Masson's trichrome and Verhoeff's staining showed excellent ECM deposition and reconstruction progressing from the sites of anastomosis towards the midpoint of implanted scaffolds. Endothelial re-coverage has also been detected during reconstruction periods. Molecular biology analysis showed increased gene expression of VSMC markers, such as SM22-α, CNN-1, and MYH-11, in the inner layer compared to native vasculature. We believe that we have developed an effective vascular graft producing platform to generate mature small diameter blood vessels that can function in animal models.

CARDIOVASCULAR #12

Role of Krüpple-like Factor 11 in Arterial Thrombosis

Wenying Liang (1), Yanbo Fan (1), Haocheng Lu (1), Jinjian Sun (1), Ziyi Chang (1), Wenting Hu (1), Huilun Wang (1), Tianqing Zhu (1), Jintao Wang (1), Jifeng Zhang (1), Reheman Adili (2), Daniel Eitzman (1), Michael Holinstat (2), Y Eugene Chen (1)

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2. Department of Pharmacology, University of Michigan Medical Center

BACKGROUND: Emerging studies have indicated the important link between vessel wall and thrombosis, while the precise mechanisms mediating the injured vessel wall-induced arterial thrombosis remain largely unexplored. Krüpple-like Factor 11 (KLF11) regulates lipid and glucose metabolism, inhibits endothelial inflammation, and has beneficial effect on stroke. However, the role of

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KLF11 in thrombotic homeostasis and arterial thrombosis remains unknown.

METHODS: We applied ferric chloride-induced carotid arterial thrombosis model in Klf11 global knockout (Klf11 KO) mice. Occlusion time was tested in Klf11 KO and wild-type mice transplanted with or without wild-type bone marrows. The expression of Klf11 and TF was detected by immunohistochemistry in the thrombotic carotid artery. Adenovirus-mediated KLF11 overexpression and siRNA-mediated Klf11 knockdown strategies were applied in human aortic smooth muscle cells (HASMCs). The expression of Klf11 and TF in culture cells were determined by qPCR and western blotting.

RESULTS: Klf11 expression was increased in the mouse thrombotic carotid artery. The occlusion time in Klf11 KO mice was significantly reduced in ferric chloride-induced arterial thrombosis compared to wild-type mice. No significant difference in bleeding time was observed in the Klf11 KO mice and control mice. Bone marrow transplantation did not reverse the pro-thrombotic status in Klf11 KO mice. Mechanistically, TF expression was elevated in the aortic smooth muscle cells from Klf11 KO mice. KLF11 overexpression reduced thrombin-induced TF expression in HASMCs. Consistently, Klf11 deficiency enhanced TF expression. In reporter gene assays, we found that KLF11 potently inhibited TF promoter-driven luciferase activity.

CONCLUSIONS: Our data demonstrate that KLF11 inhibits arterial thrombosis by regulation of TF in smooth muscle cells, suggesting that KLF11 constitutes a novel molecular target to modulate thrombosis susceptibility.

FUNDING SOURCES: This work was partially supported by NIH grants HL068878, HL137214, and HL134569 (Y.E.C.), HL138094 (Y.F.), HL138139 (J.Z.), and American Heart Association grants 18PRE34000005 (W.L), 14SDG19880014 (Y.F.) and 17PRE33400179 (H.L.).

CARDIOVASCULAR
#13

Vascular Smooth Muscle Cell Tfeb Deletion Promotes Abdominal Aortic Aneurysm

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BACKGROUND: Abdominal aortic aneurysm (AAA) is a vascular disease with a very high mortality rate in the case of rupture. Transcription factor EB (TFEB) is emerging as a master regulator of autophagy and lysosomal biogenesis. Recent studies demonstrated that TFEB has anti-inflammatory and anti-atherosclerotic effects. However, the role of TFEB in AAA remains to be explored.

METHODS & RESULTS: TFEB was down-regulated in human aortic aneurysmal lesion compared with the non-lesion area by qRT-PCR and immunostaining. Utilizing VSMC-specific TFEB deficiency (floxed-TFEB/myh11-ERT2 cre+) mice, we determined the effect of TFEB on AAA formation in vivo. In the mouse AAA model induced by the combination of AAV-PCSK9 D337Y (gain-of-function mutation) and angiotensin II infusion, VSMC TFEB deletion significantly increased abdominal aneurysm incidence and maximum aortic diameter (n =15-16 for each group, $p< 0.05$). Moreover, we observed similar phenotype in the mouse aneurysm model induced by the angiotensin II plus 3-aminopropionitrile infusion. VSMC TFEB deficiency significantly increased aneurysm formation, rupture, and mortality in this distinct aneurysm model (n =13-14 for each group, $p< 0.05$). In human aortic smooth muscle cells (HASMCs), TFEB mRNA and protein abundance were decreased upon stimulation with pro-inflammatory factors. Adenovirus-mediated TFEB overexpression inhibits VSMC inflammation and apoptosis. A consistent phenotype was observed in the TFEB knockdown HASMCs. Mechanistically, TFEB upregulated autophagy and increased B-cell lymphoma 2 (Bcl2) expression. Inactivation of Bcl2 by its inhibitors (ABT-199 or Navitoclax) abolished the anti-apoptotic effect of TFEB in HASMCs. TFEB upregulated Bcl2 at the transcriptional level and directly bound to the Bcl2 promoter measured by reporter gene and chromatin immunoprecipitation assays.

CONCLUSIONS: Our data reveal a protective role of TFEB in VSMC homeostasis, suggesting that TFEB constitutes a novel molecular target to treat aortic aneurysm.

CARDIOVASCULAR
#14

Identify Smooth Muscle Cell Specific Protein as Biomarkers for Early Diagnosis of Acute Aortic Dissection

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BACKGROUND: Aortic aneurysm and dissection are life-threathening diseases, accounting for 1 to 2% of total deaths in the Western countries. Specific and sensitive biomarkers are needed for characterization of acute aortic dissection. This study aimed to identify elevated proteins in the serum in patients of Acute Aortic Dissection (AAD).

METHODS: Serum from 7 patients with acute aortic dissection were recruited. Serum from 7 healthy volunteers and 4 patients with acute coronary syndrome confirmed by elevated TNI and ECG were used as control. Proteomics were performed on each sample.

RESULTS: 3 proteins including mycolin (MYOC), fatty-acid binding protein 4 (FABP4), fibrinogen gamma chain (FGG), were significantly up regulated in patient group. The protein that differently expressed in AAD patients were mainly involved in cell proliferation, adhesion and thrombosis.

CONCLUSIONS: MYOC, FABP4, FGG were potential biomarkers for diagnosis of AAD.

CARDIOVASCULAR
#15

Human Neonatal Thymus MSCs Promote Neovascularization and Cardiac Regeneration

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ABSTRACT: Newborns with critical congenital heart disease are at significant risk of developing heart failure later in life. Because treatment options for end-stage heart disease in children are limited, regenerative therapies for these patients would be of significant benefit. During neonatal cardiac surgery, a portion of the thymus is removed and discarded. This discarded thymus tissue is a good source of MSCs that we have previously shown to be proangiogenic and to promote cardiac function in an in vitro model of heart tissue. The purpose of this study was to further evaluate the cardiac regenerative and protective properties of neonatal thymus (nt)MSCs. We found that ntMSCs expressed and secreted the proangiogenic and cardiac regenerative morphogen sonic hedgehog (Shh) in vitro more than patient-matched bone derived MSCs. We also found that organoid culture of ntMSCs stimulated Shh expression. We then determined that ntMSCs were cytoprotective of neonatal rat cardiomyocytes exposed to H2O2. Finally, in a rat left coronary ligation model, we found that scaffoldless cell sheet made of ntMSCs applied to the LV epicardium immediately after left coronary ligation improved LV function, increased vascular density, decreased scar size and decreased cardiomyocyte death four weeks after infarction. We conclude that ntMSCs have cardiac regenerative properties and warrant further consideration as a cell therapy for congenital heart disease patients with heart failure.

CARDIOVASCULAR
#16

Cross-talk Between Transforming Growth Factor-beta and MyD88 Signaling Pathways in Vascular Smooth Muscle Cells

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BACKGROUND: Thoracic aortic aneurysm (TAA) is life-threatening disease and the death rate is about 70% among untreated patients. About 25% of the patients are linked to known genetic syndromes and aberrations in transforming growth factor-beta (TGF-β) signaling pathways. TGF-β signaling is essential for TAA progression and contributes to early stage of aneurysm development. MyD88, an innate immune adaptor protein, is critical in arterial vascular remodeling and hypertension. Cross-talk between

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TGF-β and Toll-like receptors, signaling components of innate immune system has been reported. In this study, we investigate how pharmacological inhibition of MyD88 changes the gene expression of TGF-β down-stream signaling using in vitro vascular smooth muscle cells (vSMC) culture models.

METHODS: We cultured mouse vSMC, either immortalized MOVAS-1 cells or primary vSMC isolated from ascending or descending aorta. Cells were starved in 1% FBS/DMEM for 24 hrs and then were pre-treated with MyD88 inhibitor (5~20 μM of ST2825) for 1 hr prior to TGF-β stimulation (1 ng/ml) for 3 hrs. Reverse-transcription-PCR was performed to detect gene expressions of matrix metalloproteinase (MMP)-2, MMP-9, c-jun, c-fos, serpine-1, thrombospondin (TSP)-1, interleukin (IL)-6, vascular endothelial growth factor-alpha (VEGF-α), and tumor necrosis factor-alpha (TNF-α).

RESULTS: TGF-β augmented the expressions of the genes tested in the study up to 2 ~ 10 times except MMP-2. ST2825 showed (1) dose-dependently complete inhibition (MMP-9, c-jun, c-fos, TSP-1) or partial inhibition (Serpine-1, TNF-α), (2) dose-independent partial inhibition (IL-6), (3) no effect (VEGF-α).

CONCLUSIONS: MyD88 inhibition modulates the gene expression of TGF-β down-stream molecules showing that targeting MyD88 may have therapeutic potential in treatment of cardiovascular disease such as TAA. Further studies using animal models are needed to verify the treatable effect of MyD88 inhibition on TAA. In addition, differential regulation of MyD88 on IL-6 will be of interest for understanding distinct role of MyD88 in different disease settings (TAA vs. inflammatory diseases).

CARDIOVASCULAR

#17

Transforming Growth Factor-β type 1 Receptor Gene Mutations Impairs Neural Crest Stem Cell-derived Smooth Muscle Cells Differentiation from Human Pluripotent Stem Cells

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INTRODUCTION: Loeys-Dietz syndrome (LDS) is an autosomal dominant genetic disease affecting the connective tissue in multiple human organs and is primarily characterized by thoracic aortic aneurysm (TAA). Heterozygous missense mutations in different genes of TGF-β signaling, including TGFBR1, have been detected in the patients of LDS/familial TAA. The mechanism of TGFBR1 mutation causing TAA is unknown. In this study, we analyzed the mutation of TGFBR1 (A230T) that we identified in a family of LDS/TAA by using technologies of iPSCs and CRISPR/Cas9-dependent gene editing.

HYPOTHESIS: We hypothesize that the heterozygous missense mutation of TGFBR1A230T impairs the vascular smooth muscle cells (VSMCs) differentiation from hPSCs.

METHODS: We first created heterozygous knock-in mutation of $TGFBR1^{A230T}$ into normal human embryonic stem cells (hESCs) using CRISPR/Cas9. We also generate human induced pluripotent stem cells (hIPSCs) from two patients of a family with the same mutation of $TGFBR1^{A230T}$. Through chemical defined in vitro VSMCs differentiation from hPSCs-derived neural crest stem cells, a comparison study has been performed with both iPSCs from one family member without mutation and two patients of $TGFBR1^{A230T}$ as well as hESCs with and without heterozygous knock-in point mutation of $TGFBR1^{A230T}$.

RESULTS: The differentiation of hPSCs to NCSCs was normal. However, the differentiation of NCSC to VSMCs was impaired as manifested by significant decreased expression level of myosin heavy chain 11 (MYH11), a critical VSMCs marker in late stage of VSMCs differentiation, in VSMC derived from hIPSCs/NCSCs of $TGFBR1^{A230T}$ patients compared to ones from a normal person. Compared to control hESCs with isogenic background, a significant lower expression level of MYH11 was also identified in VSMCs derived from hESCs with knock-in $TGFBR1^{A230T}$ mutation.

CONCLUSION: $TGFBR1^{A230T}$ missense mutation in both patients' hIPSCs and knonk-in hESCs cause the defect of MYH11 expression in NCSC-derived VSMCs, which may contribute to the TAA in Loeys-Dietz syndrome patients.

CARDIOVASCULAR
#18

Endothelial KLF11 Prevents Abdominal Aortic Aneurysm Formation via Inhibiting Endothelial Cell Inflammatory Activation

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BACKGROUND: Endothelial Cell (EC) inflammation contributes to many vascular diseases. Krüppel like factor 11 (KLF11), a transcription factor involved in Diabetes, inhibits EC inflammatory activation via NF-κB signaling pathway. Abdominal aortic aneurysm is a permanent dilatation of abdominal aorta and pathologically characterized by vascular inflammation, extracellular matrix degradation, vascular smooth muscle cell apoptosis. However, the protective function of KLF11 in aortic aneurysm still remains unclear.

METHODS & RESULTS: KLF11 can be induced by pro-inflammatory stimuli in vascular endothelial cells. Adenovirus-mediated KLF11 overexpression in ECs inhibits TNF-α-induced pro-inflammatory adhesion molecules expression, such as VCAM-1, ICAM-1, E-selectin, MCP-1, IL-6. Accordingly, knockdown of KLF11 with adenovirus augments the pro-inflammatory status in ECs. In vivo studies reveal that conventional KLF11 knockout (KLF11-/-) mice exhibit a significant increase in leukocyte recruitment to EC after LPS administration, Moreover, the elastase-induced abdominal aortic aneurysm (AAA) were used onto the infrarenal aorta of 8-12-week-old EC specific KLF11 knockout mice (KLF11f/f-Tie2Cre+) and littermate mice (KLF11f/f-Tie2Cre-). As results, KLF11 deficiency in ECs markedly increases elastase-induced AAA formation, aorta dilation, elastin degradation and inflammatory cells infiltration.

CONCLUSIONS: Our study indicates that KLF11 deficiency in ECs aggravates AAA development via activation of EC inflammatory response.

GI/LIVER
#19

GPC3 Targeted Nanotechnology for Hepatocellular Carcinoma Therapy

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BACKGROUND: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world with increasing incidence. Most patients undergo surgical resection, but the incidence of tumor recurrence is over 50% and patients with HCC have a poor 5-year survival rate. Chemotherapy is required for HCC patients after receiving surgical resection. Serious off-target induced side effects and systemic toxicity limit the clinical utility of drugs. Targeting therapeutic nanomedicine is an innovative strategy for enhancing drug delivery efficiency and reducing side effects. Glypican-3 (GPC3) is highly specific for HCC and is not found in non-neoplastic liver. In our preliminary data, we have found GPC3 to be overexpressed in about 90% of patients with HBV-derived HCC.

AIMS: To formulate and characterize GPC3 peptide-labeled nanoparticles encapsulating sorafenib and evaluate efficacy of nanoparticles to regress HCC xenograft tumors.

METHODS: Nanoparticles are formulated that partition sorafenib, a hydrophobic drug in the core by self-assembly. Nanoparticles will be labeled with GPC3 peptide to provide precision delivery. The properties of nanoparticle will be valued using the following methods: dynamic light scattering (DLS), transmission electron microscopy (TEM), entrapment efficiency (EE) and drug release. We will then monitor regression of tumor size in 4 groups of animals with HCC xenograft tumors treated with GPC3-labeled and scramble peptide labeled nanoparticles encapsulating sorafenib, free sorafenib, and control. Efficacy and toxicity of each therapy will be evaluated using a linear mixed effects regression model.

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RESULTS: We successfully synthesized and purified GPC3 peptide. Nanoparticles have been formulated and characterized. We expect to observe greater regression in dimensions of HCC tumor from GPC3-labeled compared with scramble peptide labeled nanoparticles, free drug, and control. And less toxicity from GPC3-labeled is expected versus unlabeled nanoparticles and free drug on necropsy.

CONCLUSION: GPC3 peptide has been successfully synthesized to produce deeper tumor penetration and local drug concentration. Nanoparticles were designed to encapsulate highly hydrophobic drugs, such as sorafenib, which is FDA approve for treatment of HCC. Improved aqueous solubility, increased drug payload, lengthened plasma half-life, and extended drug release will be characterized. Pre-clinical efficacy will be evaluated by ability to induce regression of patient-derived HCC xenograft tumors.

GI/LIVER
#20

Fat Accumulation, Liver Damage and Metabolic Abnormalities in Chinese Patients with Moderate/Severe Hepatic Steatosis

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BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) comprises a spectrum from mild to severe steatosis, and from steatosis alone to steatohepatitis, cirrhosis and liver cancer. We compared quantity and quality of fat depot in subcutaneous, visceral and muscle compartments, liver damage, and prevalence of metabolic abnormalities between Chinese NAFLD patients with moderate/severe hepatic steatosis vs. those with mild hepatic steatosis.

METHODS: NAFLD patients were prospectively recruited from Peking University in Beijing, China. All patients had baseline body composition measurements using CT and analytic morphomics, clinical evaluation, labs and Fibroscan® controlled attenuation parameter (CAP) and liver stiffness measurement (LSM). Moderate/severe hepatic steatosis was defined as CT liver attenuation ≤40 HU (Hounsfield unit). Calorie intake and physical activity were based on self-report.

RESULTS: As of April 2018, 136 NAFLD patients have been recruited, 46% men, median age 46 years, 52% had normal BMI, 23% were diabetic, and 56% had metabolic syndrome (MS). 48 (36%) had moderate/severe steatosis including 37.5% with normal BMI. Patients who had moderate/severe steatosis had higher BMI (29 vs. 24), waist circumference, ALT, prevalence of MS (71% vs.48%), CAP (333 vs. 272) and LSM compared to those with mild steatosis. They also had bigger visceral fat area (178 vs. 134 cm2) and lower visceral fat attenuation (-109 vs. -107 HU) but no difference in subcutaneous fat area, subcutaneous fat attenuation, skeletal muscle attenuation, or relative low-density muscle area. Their calorie intake was higher (1625 vs.1422 Calories/day) and time spent on physical activity was lower (160 vs. 275 minutes/week).

CONCLUSION: NAFLD patients with moderate/severe steatosis were more obese and had higher prevalence of MS. They had more visceral but not muscle or subcutaneous fat. They also had more liver damage based on labs and Fibroscan®. Counseling on diet and physical activity is important in NAFLD patients with moderate/severe steatosis including those with normal BMI.

FUNDING: This study is funded by the Michigan Medicine-Peking University Health Sciences Center Joint Institute for Translational and Clinical Research.

GI/LIVER #21

Nitro-fatty Acids Protect Against Steatosis and Fibrosis During Development of Nonalcoholic Fatty Liver Disease

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ABSTRACT: Nonalcoholic fatty liver disease (NAFLD) and resulting nonalcoholic steatohepatitis (NASH) are reaching global epidemic proportions. However, lack of non-invasive diagnostic tools and effective therapies constitute two of the major hurdles for a bona fide treatment and a reversal of NASH progression and/or regression of the disease. Nitro-fatty acids (NO2-FA) have been proven effective in multiple experimental models of inflammation and fibrosis. Thus, the potential benefits of in vivo administration of NO2-FA to treat advanced NAFLD was tested in a model of long-term NASH diet-induced liver damage. Non-invasive imaging approaches were pursued, to establish advanced experimental models of NASH in which both steatosis and fibrosis were diagnosed prior experimental therapy with nitro-oleic acid (OA-NO2). Experimental controls included delivery of equimolar amounts of the non-nitrated oleic acid (OA). CLAMS and NMR-based analysis demonstrates that OA-NO2 improves body composition and energy metabolism and inhibits triglycerides (TG) accumulation in the liver with no major effect on cholesterol homeostasis. Photoacustic ultrasound (PA-US)-based imaging revealed a robust inhibition of liver steatosis and fibrosis (collagen deposition) by OA-NO2. These results were further supported by histological analysis and quantification of lipid accumulation, lobular inflammation (F4/80 staining) and fibrosis (αSMA staining) as well as established parameters of liver damage (ALT). In vitro studies using primary hepatocytes and HepG2 cells indicated that OA-NO2 inhibits TG biosynthesis and accumulation and inhibits fibrogenesis in human stellate cells. Bioinformatic analyses further revealed a significantly association between key genes involved in inflammation and fibrosis modulated by OA-NO2 in the NASH experimental model with hepatic steatosis and NASH progression in humans. Taken together, our studies demonstrate that NO2-FA improve steatohepatitis and fibrosis and may constitute an effective therapeutic approach against advanced NAFLD that warrants further clinical evaluation.

GI/LIVER #22

Microdroplet-enabled Profiling of Human Gut Microbial Consortia Utilizing Resistant Starch

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ABSTRACT: Enhanced short-chain fatty acid (SCFA) production by the gut microbiome through supplemented dietary fiber has been demonstrated to alleviate metabolic syndrome and certain disease phenotypes, such as type 2 diabetes mellitus (T2DM). However, due to the limited resolution of current microbiome profiling tools, studying the specific network of microorganisms responsible for this fiber utilization and their ecological interactions in an individual has not been accomplished. To address this technological gap, we present a highly parallel and high-throughput microfluidics-based approach capable of elucidating fiber degrading and fermenting microbiota. We first demonstrate this capability with the co-cultivation and study of a simple model consortium - composed of a highly efficient starch degrader, a fermenter producing SCFA from released saccharides, and a syntrophic methanogen - capable and representative of resistant starch utilization in the human gut. In the future, we plan to

use this microfluidic capability as a platform to screen an individual's microbiota for similar consortia capable of resistant starch utilization by generating and co-cultivating thousands of microdroplets with granules of resistant starch, bacterial populations from a sample from an individual, and a spike-in of a biosensor.

PULMONARY
#23

Short-term Exposure to High Ambient Air Pollution Aggravates Respiratory Symptom and Lung Function in Asthma Patients in Bejing, China

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BACKGROUND: Air pollution can cause acute exacerbation of asthma. We aimed to investigate the short-term respiratory effects of ambient air pollution in asthma patients in the context of high pollution levels in Asian cities.

METHODS: A panel of 32 asthma patients was recruited and repeatedly recorded for asthma control test (ACT) score , and measured for lung function in November 2015 - December 2016 . Daily ambient air pollution data including $PM_{2.5}$, PM_{10}, SO_2, NO_2 and CO were obtained from nearby central air-monitoring stations. Mixed effects models in R 3.3.2 were used to estimate the associations between exposures and health measurements with adjustment for potential confounders.

RESULTS: We collected repeated clinical data every 1 month for 2 to 13 times for 32 asthma patients (totally 266 visits). Interquartile range (IQR) increase in $PM_{2.5}$ (74.5 μg/m3, 6-d), PM_{10} (78 $\mu g/m^3$, 5-d), SO_2 (10 $\mu g/m^3$, 7-d), NO_2 (37 $\mu g/m^3$, 6-d), CO (0.7 $\mu g/m^3$, 6-d) were significantly associated with reduction in ACT score of 3.6 % (95% CI: -6.3%, -0.9%) , 2.8% (95% CI:-5.1%, -0.5%) , 3.2 % (95% CI: -5.5%, -0.9%), 3.8% (95% CI:-7.0%, -0.5%) and 2.9 % (95% CI: -4.3%, -1.4%), respectively. An IQR of 78$\mu g/m^3$ in 7-d PM_{10} moving average concentrations were significantly associated with a 3.6% (95%CI: -5.6%, -1.5%) reduction in FEV1%.

CONCLUSIONS: Our results provide potential important public health implications that ambient air pollution may aggravate respiratory symptoms and lung fuction of asthma patients in Beijing, China.

FUNDING: Michigan Medicine-Peking University Health Science Center Joint Institution for translational and Clinical Research.

RENAL
#24

Genome-wide Association Study of IgA Nephropathy, IgA Vasculitis and lupus Nephritis

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Poster Abstracts
海报内容摘要

BACKGROUND: IgA nephropathy (IgAN), lupus nephritis (LN) and IgA vasculitis (IgAV) are three types of glomerulonephritis (GN) with high prevalence in both Chinese and American populations, leading to end-stage renal disease (ESRD). We hypothesize that IgAN, LN and IgAV must share common and disease-specific genetic variant regions and that fine mapping of those regions and replication in independent cohorts will highlight most relevant single nucleotide polymorphisms associated with those three autoimmune renal diseases.

METHODS: Standard quality control of the GWAS data were performed using the following criteria: removing samples with genotyping rate <95%, discordant gender information; outlying heterozygosity rate, duplicated or related individuals, and sample outliers based on PCA method (continental and sample PCA) and removing markers with call rate <98%, deviated from H-W equilibrium in controls($p<0.000001$), batch difference, different missing genotype rates between cases and controls, and MAF <1%. Imputation was done using the Michigan Imputation Server with 1000 Genomes Phase 3 as reference, and included only markers with imputation r^2 >0.7. Meta-analysis was conducted using METAL software.

RESULTS: Our study is one of the largest IgAN GWAS from the same center, avoiding renal biopsy heterogeneity. After quality controls, a genome-wide analysis was performed in 2,747 biopsy-confirmed cases and 3,952 controls, including 3 new cohorts comprising 1,553 cases, 3,050 controls of European ancestry and the previously published Han Chinese discovery cohort of 1,194 cases and 902 controls. Top signals, defined by association $P < 5 \times ^{10-5}$, were genotyped in an additional 4,911 cases and 9,002 controls, and a meta-analysis was performed to identify genome-wide significant signals across the combined cohorts of 20,612 individuals. The METAL heterogeneity analysis has been completed for 9,020,572 markers. The smallest p-value was 1.055e-22.

SUMMARY: Additional loci and novel genes for genetic predisposition to IgAN were revealed, which may shed novel biological mechanisms.

FUNDING: We thank the Michigan Medicine - PKUHSC Joint Institute for supporting our work.

RENAL
#25

Transcriptional Profiling Identifies STAT1-driven Signaling and Candidate Disease Biomarkers in Vasculitis

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BACKGROUND: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is one of the most common autoimmune diseases in adults. Left untreated, the majority of patients succumb to disease within a year. The current study tested the hypothesis that transcriptional profiling would identify potential biomarkers that could have prognostic or predictive applications for patients with AAV.

METHODS: Transcriptomic profiles were generated from microdissected compartments of kidney biopsies from 80 patients with AAV using the European Renal cDNA Bank (ERCB); profiles from patients with AAV and other renal indications were compared to healthy living donors.

RESULTS: In previous analyses, EGF was negatively associated with eGFR in AAV ($r=0.71$, $p<0.001$) and urinary EGF/Cr level was independently associated with the end stage renal disease (ESRD) or 30% reduction of eGFR. In the tubulointerstitium, 734 differentially expressed genes (DEGs) were shared in AAV and other renal indications. Functional analysis of upstream transcriptional regulators identified 21 regulators with predicted activation; STAT1 ($p=5.9E-12$, Z-score=4.6) demonstrating the highest predicted activity. Genes downstream of STAT1 activation were assessed for their potential use in biomarker studies and included C3, TP53, and LCN2, all were negatively correlated with eGFR in AAV and CKD ($p<0.001$). Independently of upstream regulators, 166 DEGs were identified as candidate biomarkers, 27 of which were highly expressed in AAV and negatively correlated with eGFR across CKD ($p<0.001$), including ANXA1 and TIMP1.

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CONCLUSION: Prognostic and response biomarkers can be identified in AAV through assessment of transcriptional profiling, as has been exemplified by uEGF. AAV-relevant transcriptional profiles shared across CKD identified numerous transcriptional regulators including STAT1, implicating JAK-STAT pathway activation in AAV as has been shown in other renal diseases. Feasibility studies assessing candidate biomarkers in AAV and CKD are ongoing.

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RENAL
#26

Mitochondrial Nutrient Metabolism and Progression of Chronic Kidney Disease

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ABSTRACT: Chronic kidney disease (CKD) is a significant public health problem. Progression to end-stage renal disease (ESRD) leads to dramatic increases in morbidity and mortality. The mechanisms underlying progression of CKD are poorly defined and current noninvasive markers incompletely correlate with disease progression. In our previous work, we found that Tamm Horsfall Protein (THP) increased in the urine in a rodent hypoxia-induced kidney injury model, with increased THP associated with protection from injury. Our recent human studies indicate that altered tubular mitochondrial nutrient metabolism, specifically higher levels of tricarboxylic acid (TCA) cycle intermediates, predicts progression of diabetic kidney disease (DKD). In contrast, lower urinary THP levels associate with human CKD progression. In this proposal, we seek to link THP levels to mitochondrial function, identifying a protective role of THP on renal disease progression by utilizing complimentary rodent and human studies in DKD. We will utilize a THP-/- rat model to determine the effect of THP on mitochondrial nutrient metabolism and DKD severity. In parallel experiments, we will assess the relationship between urinary nutrient metabolites and urinary THP levels, and determine if either or a combination of these are markers of DKD progression. For this, we will utilize samples from our existing biobanks with 50 subjects from Peking University Health Sciences Center and 50 subjects from the Clinical Phenotyping Resource and Biobank Core at the University of Michigan. In each cohort, the 50 subjects will comprise of 25 who progressed (doubling of serum creatinine or ESRD) and 25 who did not progress over the duration of 1-5 years of follow-up, matched for demographic and clinical features. These discovery studies will lay the groundwork for future large-scale prospective studies to identify the biomarker potential of urinary THP and TCA cycle metabolites and mechanistically define the link between THP and mitochondrial function.

PSYCHIATRY
#27

Improving Physical Health and Functioning in Substance-dependent Adults with HIV/AIDS and Chronic Pain

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ABSTRACT: Psychological interventions have demonstrated efficacy for reducing pain and improving functioning in persons with a broad spectrum of pain-related conditions. This study is based on the premise that addressing pain-related use of substances may be a way to modify substance use and improve mental and physical health outcomes in adults treated for SUDs who also have HIV/AIDS. An existing CBT/ACT intervention provides a theoretically sound and potentially useful foundation on which to build a specific intervention for adults with HIV/AIDS. However, the public health impact of the intervention will be enhanced by: (a) conducting culturally-appropriate content to highlight common sources of pain in those with HIV/AIDS; (b) explicitly discussing side effects of HIV/AIDS medications and highlighting the importance of adherence to these medications; (c) addressing the role of substance use in facilitating HIV risk behaviors; and (d) addressing how substance use can interfere with HIV/AIDS

treatment adherence. Refining CBT/ACT intervention will make a significant impact because it could (1) decrease pain and substance use, (2) improve quality of life, and (3) decrease the costs to society of poorly managed HIV/AIDS and engagement in HIV risk behaviors. It is worth noting that the vast majority of behavioral intervention research has been conducted in the US or within English-speaking countries. The proposed study will simultaneously develop the intervention and translate the content into Mandarin for use in a future large-scale randomized clinical trial to test the impact of the CBT/ACT intervention on chronic pain, functioning, substance use and HIV/AIDS treatment adherence in a high risk inner city population in both the US and China. This project will lay the groundwork for future funded joint research by UM and PKU faculty.

OB/GYN
#28

3D Stress MRI-based Structural Failure Pattern and Biomechanical Analysis Comparing Chinese vs. American Women with Pelvic Organ Prolapse

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BACKGROUND: Pelvic organ prolapse afflicts from 13.1 to 25.9% in China and the US so severely that it requires surgery in ~230,000 US women per year with a 25% surgical failure even in best hands. It has been suggested that Chinese and American pelvic floor anatomy are fundamentally different, yet important differences have not been adequately studied. Additionally, parity, a primary etiologic factor in Western women, is significantly different given the 'one child policy' in China. Despite the goal of providing personalized precision pelvic floor surgery fitting women's unique function anatomy condition, data from Caucasian women are currently being used for Chinese treatment and surgical planning without knowing about differences.

OBJECTIVES: Giving the knowledge gap, our goals to Aim1) test anatomical differences hypothesis, Aim 2) compare the quantitative characteristic of structural failure frequency and pattern in cohort of Chinese and Caucasian women (prolapse vs. controls); Aim 3) and use biomechanical models to explore the effects of these difference in providing pelvic floor support.

STUDY DESIGN: We will use newly developed cutting-edge techniques combining "3D Stress MRI" with biomechanical structural analyses for both Chinese and Caucasian cohorts. Each cohort will consist of 10 nulliparous, 25 parous controls and 25 women with prolapse. Nulliparous women will be used to investigate racial anatomical difference independent of the effect of parity (AIM1). The difference between parous control and prolapse in both cohorts (Aim 2) will be compared. Biomechanical modeling analysis will be used to study their impact on pelvic floor support.

EXPECTED RESULTS: We expect that Chinese patients would have less frequent muscular failure due to low parity and have different causal factors leading to the development of prolapse. These pilot data will provide effect sizes for the sample size estimation for designing the definitive study to answer these important questions.

PROJECT PROGRESS: The team had made the significant progress on the project since the project has been funded. 1) IRBs have been approved for both PKUHSC and UMHS sites; 2) MRI scanning protocol and parameters have been adopted and adjusted at the PKUHSC radiology department and four testing scans have been collected and reviewed to ensure data quality. 3) UMHS team is developing a custom modular in 3D slicer to facilitate and streamline the data analysis process.

Poster Abstracts
海报内容摘要

OB/GYN
#29

Towards Understanding Human Embryo Mosaicism: Regional and Developmental Genetic Concordance by Single Cell Sequencing

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BACKGROUND: Knowledge of human preimplantation embryonic genetic concordance at a single cell level is essential, and wanting, to appreciate the incidence of human embryo mosaicism and interpretation of preimplantation genetic testing for aneuploidy (PGT-A) in relation and offspring genetic normalcy. We asked: how does the ploidy status compare between neighboring trophectoderm (TE) cells, neighboring inner cell mass (ICM) cells, and ICM-derived human embryonic stem cells (hESCs) at a single cell level?

METHODS: Human blastocysts were donated with informed consent to an IRB-approved study for hESC derivation. Warmed blastocysts underwent laser dissection of the ICM for hESC derivation and resulting TE was collected for single cell isolation. ICMs were plated on human foreskin fibroblasts in xeno-free media with knock-out serum replacement. After 3-4 days of culture half of the ICM was harvested for single cell isolation. Remaining ICMs were used to derive hESCs. TE, ICM, and hESC single cells were isolated with trypsin/accutase treatment, confirmed to be single cells, placed individually into tubes for lysis, and whole genome DNA amplification was performed. Single cell amplicons were confirmed by gel electrophoresis, used to make sequencing libraries, and subjected to next generation sequencing to compute copy number variance (CNV) for single cell aneuploidy detection. hESCs were also assessed by single cell G-banding. Differences in genetic concordance (%) within specific embryonic regions and/or during development of hESCs were statistically compared by X^2.

RESULTS: To date 252 single cell CNVs have been measured, comprised of 182 single cell-TEs from 19 embryos (9.6±0.8, ave±se cells/embryo), 37 single cell-ICMs from 3 embryos (12.3±3.3 cells/embryo), and 33 single cell-hESCs from 3 embryos (11.0±2.3 cells/embryo). Collectively, significantly less single cell genetic concordance ($p<0.001$) existed in TE (69%) compared to ICM (89%) and hESCs (94%). In the only 2 sample sets with TEs, ICMs, and hESCs per embryo, the per embryo/per region concordance rates were TE – (50%, n=10 and 50%, n=10), ICM – (95%, n=19 and 89%, n=9), and hESCs (100%, n=11 and 100%, n=12), respectively.

CONCLUSIONS: These data suggest that single cell genetic concordance is lower in the human TE compared to the ICM and/or resulting hESCs. These findings may have significant relevance on understanding: i) human embryo mosaicism, ii) PGT-A results obtained from multiple unknown numbers of TE cells biopsied, and iii) fidelity of TE proxy for the ICM and subsequent offspring genetic normalcy.

FUNDING: Michigan Medicine - Peking University Health Science Center Joint Institute

KINESIOLOGY
#30

Single High-fat Meal Alters Soluble RAGE Profiles and Peripheral Blood Mononuclear Cell RAGE Expression

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ABSTRACT: A high-fat diet can induce chronic low-grade inflammation and metabolic diseases such as diabetes and atherosclerosis. The receptor for advanced glycation endproducts (RAGE) plays a critical role in inflammatory signaling in metabolic disease and the soluble form of the receptor (sRAGE) can mitigate these effects. However, less is known about the role of RAGE in postprandial inflammation and the effect of exercise in this context. Thus, we aimed to determine the effects of a single high-fat

meal (HFM) with and without prior aerobic exercise on peripheral blood mononuclear cell (PBMC) RAGE biology. Healthy male participants (n=12) consumed a HFM on two separate occasions, one without prior exercise and one 16-18hrs following a bout of aerobic exercise. Total soluble RAGE (sRAGE) and endogenous secretory RAGE (esRAGE) were determined via ELISA and cleaved RAGE (cRAGE) was calculated as the difference between the two. Further, isolated PBMCs were analyzed for RAGE, ADAM10, TLR4 and MyD88 protein expression and ADAM10 activity. The HFM significantly ($p<0.01$) attenuated circulating sRAGE, esRAGE, and cRAGE by 9.7%, 6.9%, and 10.5% respectively. While the HFM increased PBMC RAGE protein expression by 10.3% ($p<0.01$), there was no meal effect on PBMC TLR4, MYD88, or ADAM10 protein expression, nor ADAM10 activity ($p= 0.2, 0.7, 0.3, 0.2$ respectively). There was also no effect of exercise on any experimental outcomes. These findings suggest that PBMCs are involved in postprandial inflammation via RAGE activation. However, due to no change in ADAM10, it is unlikely that PBMCs directly influence sRAGE production following a HFM.

KINESIOLOGY
#31

Circulating Soluble RAGE Isoforms are Attenuated in Obese, Impaired Glucose Tolerant Individuals and are Associated with the Development of Type 2 Diabetes

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ABSTRACT: The soluble receptor for advanced glycation endproducts (sRAGE) may be protective against inflammation associated with obesity and type 2 diabetes (T2DM). The aim of this study was to determine the distribution of sRAGE isoforms, and whether sRAGE isoforms are associated with risk of T2DM development in subjects spanning the glucose tolerance continuum. In this retrospective analysis, circulating total sRAGE and endogenous secretory RAGE (esRAGE) were quantified via ELISA and cleaved RAGE (cRAGE) was calculated in 274 individuals stratified by glucose tolerance status (GTS) and obesity. Group differences were probed by ANOVA and multivariate ordinal logistic regression was used to test the association between sRAGE isoform concentrations and the proportional odds of developing diabetes, versus normal glucose tolerance (NGT) or impaired glucose tolerance (IGT). When stratified by GTS, total sRAGE, cRAGE, and esRAGE were all lower with IGT and T2DM, while the ratio of cRAGE to esRAGE (cRAGE:esRAGE) was only lower ($p<0.01$) with T2DM compared to NGT. When stratified by GTS and obesity, cRAGE:esRAGE was higher with obesity and lower with IGT ($p<0.0001$) compared to lean, NGT. In ordinal logistic regression models, greater total sRAGE (odds ratio: 0.91; $p<0.01$) and cRAGE (odds ratio: 0.84; $p<0.01$) were associated with lower proportional odds of developing T2DM. Reduced values of sRAGE isoforms observed with both obesity and IGT are independently associated with greater proportional odds of developing T2DM. The mechanisms by which each respective isoform contributes to obesity and insulin resistance may reveal novel treatment strategies for diabetes.

Poster Abstracts
海报内容摘要

MICROBIOM
#32

Microdroplet Co-cultivation and Characterization of Vaginal Bacteria in Vaginal Fluid

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ABSTRACT: The human vaginal microbiome (HVM) plays a fundamental role in women's health and susceptibility to sexually transmitted infections (STIs). For instance, bacterial vaginosis (BV) is characterized by the depletion of lactobacilli and an overgrowth of fastidious and facultative anaerobes. BV is associated with infertility, preterm birth, and an increased risk of acquiring STIs like HIV. Cervicovaginal secretion (CVS) has been shown to decrease the rate of infectivity for HIV and demonstrate antimicrobial activity against nonresident bacteria. Despite the influence of CVS in the HVM, the ecological roles of many vaginal species and effects from the host still remain unclear. Current approaches for investigating them have severe limitations including a hampered ability to process small volumes of precious samples. In this work, we employed a microfluidic technology platform to encapsulate vaginal bacteria in CVS microdroplets. Our aim is to dissect bacterial inter-species interactions in the HVM while examining effects from CVS, which was also analyzed to screen for some small molecules that may contribute to inter-species interactions. Furthermore, the CVS that was used for cultivation was pooled from donors of reproductive age with similar microbial composition. Lactobacillus crispatus, a well-characterized vaginal species that is associated with promoting health in the vagina, was encapsulated in nano-liter microdroplets and underwent anaerobic incubation in CVS. Subsequently, analytical assays were carried out for characterization of these microdroplets. Our results show that microdroplet co-cultivation and characterization provide an effective means for identifying inter-species interactions in the HVM. Further extension of this approach and its future applications hold tremendous potential for novel ex vivo studies as shown in this work.

SURGERY
#33

Citrullinated Histone H3: A Novel Target for Treatment of Endotoxic Shock

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ABSTRACT: We have recently shown that citrullinated histone H3 (CitH3) is significantly elevated in endotoxemia. In the present study, we developed a novel anti-CitH3 monoclonal antibody (mAb), to determine whether neutralization of circulating CitH3 can attenuate organ dysfunction and improve survival in a mouse model of lethal lipopolysaccharide (LPS)-induced shock.

METHODS: A CitH3 peptide (citrulline R2+R8+R17+R26) was synthesized to generate a novel anti-CitH3 mAb. Binding affinity of this anti-CitH3 mAb was compared to a commercial anti-CitH3 mAb generated by a different CitH3 peptide (citrulline R2+R8+R17). C57BL/6J mice were randomized to receive (n=9/group): mouse IgG (20mg/kg, IV); LPS (20 mg/kg, IP) + mouse IgG; LPS (20 mg/kg, IP) + new anti-CitH3 mAb (20 mg/kg, IV), and LPS + commercial anti-CitH3 mAb (20 mg/kg, IV). Survival was monitored for 10 days. In a separate cohort (n=3/group), lung tissue was harvested for pathological examination. The levels of IL-1β and TNF-α in lung homogenate and blood were determined by enzyme-linked immunosorbent assay. Double-stranded DNA was measured for analysis of neutrophil extracellular trap (NET) formation. ANOVA was used for multiple comparisons and Kaplan-Meier curves for survival.

RESULTS: Compared to the commercial anti-CitH3 mAb, our new anti-CitH3 mAb demonstrated higher specificity and binding affinity to CitH3. LPS insult increased levels of the pro-inflammatory cytokines in lung and blood, stimulated NET formation, and caused severe acute lung injury. Treatment with the new CitH3 mAb, but not commercial CitH3 mAb, attenuated LPS-induced alteration and improved survival significantly ($P<0.05$).

CONCLUSIONS: We have demonstrated for the first time that a specific anti-CitH3 mAb can bind to CitH3 with higher affinity compared to commercial anti-CitH3 mAb; and that the treatment with this novel mAb can improve outcomes following lethal LPS injection. CitH3 may be a potential therapeutic target for the treatment of sepsis in the future.

FUNDING: This work was sponsored by a Michigan Medicine - PKUHSC Joint Institute grant.

SPORTS MEDICINE

#34

Multifactorial Assessment of Articular Cartilage Injury and Remodeling after Anterior Cruciate Ligament Rupture and Reconstruction

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BACKGROUND: Post-traumatic osteoarthritis (PTOA) is the consequence of traumatic joint injury, acute inflammation, and chronic changes in joint biology. Rupture of the anterior cruciate ligament (ACL) is a major risk factor for the development of PTOA, but the precise etiology of PTOA following ACL rupture is not yet known. Surgical ACL reconstruction does not mitigate the incidence of PTOA development, although it successfully restores function. Quantitative molecular and imaging biomarkers may provide new insights into the natural history of cartilage degeneration following this injury and treatment.

METHODS: We will undertake a prospective cohort of 38 patients undergoing primary ACL reconstruction after rupture. We will assess longitudinal progression of patient-reported outcomes, knee laxity, MRI-based articular cartilage morphology and composition, and serum biomarkers of cartilage degeneration up to 1 year of follow-up. Stem cell mobilization, chemokine and cytokine concentrations, and inflammatory cell recruitment into synovial tissue will be measured from intraoperatively-collected samples. Mixed multivariate linear regression modeling will elucidate novel relationships between patient demographics, anatomy, biological factors, and downstream alterations in articular cartilage morphology and composition. Patient recruitment will be evenly split between UM and PKUHSC.

RESULTS: We gratefully received funding from the JI end of June 2018. We are now rigorously optimizing our quantitative MRI protocol using phantoms and preliminary volunteers, which will facilitate accurate longitudinal comparison of our collective patients. Unanticipated MRI scanner software upgrades have delayed us slightly. We expect to begin enrollment in September 2018.

CONCLUSIONS: We expect to observe that patients with longitudinally-increased MRI-based cartilage surface roughness exhibit greater pain, slower functional recovery, and greater serum biomarker concentrations. Knee laxity is expected to correlate strongly with biomarker concentrations given altered, adverse joint loading. These novel associations will act as critical preliminary data for large-scale funding while forming the basis for potential novel prognostic factors for this very common sporting injury.

FUNDING: We are grateful for support from the Michigan Medicine-PKUHSC Joint Institute.

Poster Abstracts
海报内容摘要

PHARMACOLOGY
#35

Identification of Potassium Channel Variants in Epileptic Encephalopathy Patients

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ABSTRACT: The goal of our work is to understand the mechanism of variants in potassium channel genes linked to pediatric epileptic encephalopathy. Variants identified in potassium channel genes in a cohort of 300 Chinese pediatric patients will be expressed in heterologous cells to determine how mutations affect ion channel activity. Potassium channel variants were identified and confirmed in two steps. First, a group of 93 potassium channel genes was identified and chosen for analysis. Genomic DNA samples were extracted from the epileptic encephalopathy patients and their parents. DNA libraries were constructed from the genomic samples in the patient cohort, and were captured using the panel of potassium channel genes. In the second step, captured DNA sequences were sequenced using paired end sequencing. After sequencing, we compared reads to the human reference genome build hg19 to identify variants. We tested parental origins for all validated variants and conducted segregation analysis in families as possible. The patient cohort had 75 variants in 10 different genes. Of these 75 variants, 54 were found to be unique to this study. The largest numbers of variants were identified in KCNQ2 (32/75), followed by KCNT1(21/75), and KCNMA1(9/75). The nine variants that we identified in KCNMA1 were de novo, and all have been classified as potentially damaging. Working with a collaborator at the University of Maryland, we have obtained a cDNA expression clone of KCNMA1 for expression of these variants in mammalian cells. In summary, using a non-biased approach, we have identified a series of variants in potassium channel genes that are linked to epileptic encephalopathy in a Chinese cohort of patients. We have prioritized 9 variants in KCNMA1 for further functional analysis.

BIOMEDICAL INFORMATICS
#36

Mapping of Chinese Emergency Department Patient Records to Standard Medical Ontologies

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ABSTRACT: A major obstacle for analyzing large volumes of Chinese medical records is the variations of medical terms for same symptom, diagnosis and treatment from different hospitals and doctors. Although organizations and companies in China developed various solutions for electronic records and clinical data mining, there are many compatibility issues. There is no overarching conceptual framework in China for combining medical data with those from other parts of the world, either.

We propose to map Chinese medical terms to widely adopted medical ontologies such as the Unified Medical Language System (UMLS). UMLS is a long-term research and development project initiated by the US National Library of Medicine in 1986. It is designed to link different text strings, used by different people and databases, to over 3 million unique biomedical concepts in ontologies for ~ 200 sources including ICD-10, SNOMED and MeSH.

To develop a proof-of-concept solution, the JI Biorepository and Bioinformatics Core are collaborating with the PKUHSC Third Hospital Emergency Department for the automated mapping their patient

records to ICD-10 through three steps: 1) use batch translation results from Google, Bing and Baidu and the subsequent mapping of translated English terms to ICD-10 concepts through our mgrep program to convert the time consuming manual translation and concept match to the much simpler multiple choice problems. 2) adopt the crowd-sourcing approach for combining choices from emergency medicine doctors and medical students for determining the correct Chinese medical term to ICD-10 mapping. 3) derive a context-dependent Chinese term to ICD-10 mapping based on crowd sourcing results for automated processing of large volumes of medical records.

Currently we finished the first stage and are working on the crowd source approach with additional funding support from PKUHSC. We are looking forward to potential collaboration in other medical areas.

BIOMEDICAL INFORMATICS

#37

Sharing of Radiology Images Containing Protected Health Information

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ABSTRACT: Several JI projects need to share dozens or hundreds of radiology images in DICOM format between PKUHSC and UM. Since the DICOM format embeds protected health information (PHI) in the metadata of the image files, it is necessary to have a solution that can ensure proper management and transmission of such images.

We developed a highly automated solution for the de-identification, encryption and transmission of large number of DICOM images through the seamless integration of functions from several open source LINUX packages. No user intervention is needed beyond 1) transfer of the files to and from JI servers 2) the generation of PGP public and private keys by the receiver.

Once the sender moves these images to a predefined folder on the JI server on the sender's side (PKUHSC or UM), our program will find all DICOM or zipped DICOM files and then automatically de-identify the DICOM files by removing the DICOM fields containing PHI. The de-identified DICOM image files will be moved to a staging folder, where they will be encrypted with the receiving user's PGP public key in batch mode and then will be moved to the transfer folder. Files in the transfer folder will be automatically synchronized to the other side of JI server (UM or PKUHSC) every five minutes using the existing JI data sharing solution that is designed to deal with unstable internet connection between PKUHSC and UM. The transferred files can only be used by the receiver with the corresponding PGP private key.

This solution can be adapted to transfer other file types that require high level of security. We can also help JI researchers to develop custom solutions to meet unique data management and analysis needs for different JI projects.

BIOMEDICAL INFORMATICS

#38

Ahub: Web-based Interactive Analysis Platform for RNA-seq Data

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ABSTRACT: The Ahub is designed to enable wet-lab biologists to perform pure GUI-based differential expression, Reactome pathway, gene set enrichment and WGCNA (Weighted Gene Co-expression Network Analysis) for RNA-seq assays. It also facilitates the validation and interpretation of statistical analysis results in the relevant biological contexts by providing interactivity between the Ahub web application and three local genomic data visualization programs: CoolMap (ontology-driven dynamic heatmap), Cytoscape (network visualization) and IGV (Integrative Genomics Viewer). Researchers can

select data points in interactive Ahub statistical plots (e.g., highly differentially-expressed genes in Ahub MA-plot) and the corresponding genes in these program(s) will be automatically highlighted through secured data exchange. Ahub will automatically generate an extensive report listing the analysis environment, packages and parameters used as well as equivalent R script (without the code related to interactivity) that researchers can use for publication or to experiment on their local RStudio for further customization.

JI researchers are welcome to use Ahub and we are committed to improve and to add more analysis functions.

CARDIOVASCULAR
#39

Extreme Levels of Air Pollution Associated with High-Density Lipoprotein Dysfunction in Healthy Adults: The Beijing AIRCHD Study

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OBJECTIVE: We aimed to assess if high levels of ambient air pollution could impair high-density lipoprotein (HDL) function and to elucidate the biological pathways involved.

APPROACH & RESULTS: In Beijing AIRCHD Study, seventy-three healthy adults (23.3 ± 5.4 years) were followed with four repeated clinical measures between November 2014 and January 2016 in Beijing. We measured ambient air pollution concentrations, along with metrics of HDL functions, and parameters of inflammation and oxidative stress. Average daily concentrations of ambient particulate matter with diameter less than 2.5 μm (PM2.5) were 84.0 μg/m^3 (6.8 to 349.2 μg/m^3). We observed significant decreases in HDL cholesterol efflux capacity of 2.3% (95% confidence interval [CI]: -4.3, -0.3) to 5.0% (95% CI: -7.6, -2.4) associated with interquartile range increases in prior up to 7 day moving averages of PM2.5 and traffic-related air pollutants (black carbon [BC], nitrogen dioxide [NO2] and carbon monoxide [CO]). Higher ambient air pollutant levels were also associated with significant reductions in circulating HDL-C and apolipoprotein A-I, as well as elevations in HDL-oxidization index, oxidized low-density lipoprotein, malonaldehyde and high-sensitivity C-reactive protein.

CONCLUSIONS: High global air pollution concentrations were associated with impairments in HDL functionality, potentially due to systemic inflammation and oxidative stress. These novel findings further our understanding of the mechanisms whereby air pollutants can promote cardio-metabolic disorders.

OB/GYN
#40

Towards Understanding Human Embryo Mosaicism: Regional and Developmental Genetic Concordance by Single Cell Sequencing

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OBJECTIVE: We are aiming to measure the incidence of human blastocyst mosaicism, and to determine the genetic concordance of mural trophectoderm (TE) biopsy and PGS results with single cell genetic analysis of inner cell mass (ICM), TE and human embryonic stem cells (hESCs).

METHODS: Human blastocysts were donated voluntarily after informed consent. Following warming and growth in vitro of blastocysts, the ICM was isolated from the TE by micro-manipulation assisted by laser-dissection. Biopsied TE and part of the ICM and was digested with accutase and trypsin-EDTA to get single cells. The left ICM was plated onto human foreskin fibroblast for hESC derivation. Single cells were transferred to lysis buffer. Whole genome amplification (WGA) with Multiple Annealing and Looping Based Amplification Cycles (MALBAC) was performed as previously described. WGA products of single cells were used to construct sequencing library with the NEBNext Ultra DNA library Prep kit for next generation sequencing at 0.3X depth with Illumina HiSeq 4000 platform. Aneuploidies were identified by analyzing the copy number variation (CNV) of ICM, TE and hESC single cells.

RESULTS: The sequencing results of TE cells show 71.88% blastocysts are mosaic (23/32), while that of ICM cells show a lower incidence of 54.55% (6/11). And sequencing results of hESCs indicate the incidence of mosaicism is 62.50% (5/8). In TE, 43.48% (10/23) of mosaicism is caused by whole chromosome duplication or deletion, 8.70% (2/23) is caused by partial chromosomal abnormalities. In the 2 samples with both TE and hESCs from the same embryos, we found the percentage of mosaicism in hESCs tend to be lower than TE (5.26% vs. 50.00% and 11.11% vs. 44.44%).

CONCLUSIONS: Most of human blastocysts are mosaic. The mosaicism may be caused by both whole and partial abnormalities of chromosome. During embryonic development, the incidence of mosaicism may tend to be lower.

FUNDING: The Michigan Medicine - Peking University Health Science Center Joint Institute for Translational and Clinical Research

GI/LIVER
#41

Small Intestine Bacteria Overgrowth, a Symptom Needs to be Exclude from Irritable Bowel Syndrome

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BACKGROUND: Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterized by recurrent abdominal pain or discomfort, alterations in stool frequency and/or stool consistency, which have been reported by patients with small intestinal bacterial overgrowth (SIBO) as well. However, the relevance of IBS and SIBO deemed uncertain and a few evidences support that

SIBO has major contribution to the pathogenesis of IBS. Given neomycin treatment to IBS patient with SIBO lead to a negative HBT and clinical improvement but no research shows the therapeutic effect of rifaxmin on HBT positive IBS patients.

METHODS: The trial was performed at Peking University Third Hospital. Eighty-four eligible patients confirmed a diagnosis of IBS-D by Rome III criteria and separated into two groups according to the lactulose hydrogen and methane breath test (LHMBT): LHMBT negative (IBS), LHMBT positive(SIBO) and healthy volunteers with LHMBT negative(HC). Consecutive patients of IBS and SIBO were administered rifaximin 0.4g twice per day orally. Clinical evaluation including IBS Symptom Severity Scores, Bristol Stool Form Scale, food frequency questionnaire and rectal barostat examination were performed. ELISA, immunohistochemistry, UPLC-MS/MS and 16S rRNA sequencing were utilized to imply the systemic and histology inflammation status, serum metabolism profiling and fecal microbial composition.

RESULTS: SIBO group have similar clinical symptoms along with lower rectal hypersensitivity compared with IBS, while IBS have more severe systemic and colon inflammatory status. Microbial composition analysis implied enriched Enterobacteriaceae family (Enterbacter, Citrobacter, E-S, Kluyrera) in IBS which lead to a leaky gut and abnormally immune system activation, nevertheless, gut microbiota in SIBO showed mild dysbiosis. The finding are intriguing as all systemic symptoms in SIBO were inproved but only diarrhea released in IBS, it might due to IBS-enriched Enterobacteriaceae even increasing after Rifaxmin treatment.

CONCLUSIONS: LHMBT positive, which imply the SIBO, have interference in therapeutic effect of Rifaxmin on IBS through gut microbial dysbiosis, it is necessary to exclude SIBO in the diagnostic criteria of IBS.

FUNDING: Michigan Medicine-Peking University Health Science Center Joint Institution for Translational and Clinical Research

PSYCHIATRY
#42

Epidemiological Characteristics and Risk Factors of Methamphetamine-Associated Psychotic Symptoms

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BACKGROUND: Methamphetamine (MA) use causes substantial social harm and is a growing public health concern. Psychosis is a key harmful consequence of MA use.

METHODS: A cross-sectional study was conducted between April, 2012 and October, 2015 among individuals for whom MA was the principal drug of use in a Compulsory Drug Detoxification Center in Beijing, Guangdong Province. Demographic, drug use and psychological characteristics were examined using a specifically-designed questionnaire, the Positive and Negative Syndrome Scale, Barratt Impulsive Scale, Hamilton Anxiety Scale and Beck Depression Inventory. Logistic regression was performed to explore the risk factors for MA-associated psychotic symptoms.

RESULTS: A total of 1685 participants were included. The prevalence of MA-associated psychotic symptoms was 17.0% among MA users during periods of abstinence. Multiple logistic regression

analyses showed that a higher dose (≥0.2 g per time) and a longer duration of MA use (>3 months), and a history of heroin use and tobacco use were associated with MA-associated psychotic symptoms, with adjusted odds ratios (ORs) of 1.96 (95% confidence interval [CI]: 1.40-2.76), 1.98 (95% CI: 1.33-2.96) and 2.45 (95% CI: 1.67-3.60), 1.78(95% CI: 1.27-2.49) respectively. MA users with anxiety and depression symptoms had significantly greater risk for MA-associated psychotic symptoms by 9.70 (6.92-13.59) and 1.90 (1.36-2.65) times respectively. Individuals with higher impulsivity were more likely to have MA-associated psychotic symptoms than those with lower impulsivity (OR=2.19; CI:1.50-3.20).

CONCLUSION: MA-associated psychotic symptoms occurred frequently among MA users in China. The efforts that facilitate attempts of drug users to reduce MA use, abstain from poly-drug use, and to control associated psychiatric symptoms and impulsivity should be supported because of their potential contribution to MA-associated psychotic symptoms in this population.

PSYCHIATRY
#43

Pattern and Change of Cognitive Impairment Associated with Psychotic Symptoms Among Methamphetamine Users During 6-month Follow-up

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BACKGROUND: Methamphetamine (MA) use causes psychotic symptoms, and prolonged exposure to MA is associated with cognitive impairment. This study aims to investigate the relationship between cognitive impairment and the severity of MA-associated psychosis, and to evaluate cognitive changes over 6 months in MA users with different psychotic severity patterns.

METHODS: A total of 528 individuals who used MA were recruited from compulsory and voluntary detoxification and rehabilitation centers in Guangdong Province, China. The neurocognitive function and psychotic symptom profiles of each participant were evaluated with the Montreal Cognitive Assessment (MoCA) and the Positive and Negative Syndrome Scale (PANSS). Participants were classified into three groups based on their PANSS scores at baseline and follow-up, including deterioration, maintenance and improvement. Changes in MoCA scores were then compared among these three groups.

RESULTS: At baseline, compared to individuals without psychotic symptoms, participants with psychotic symptoms were at higher risk of cognitive impairment (OR=1.65, 95%CI: 1.13-2.40). At 6-month follow-up, those with continuous MA use reported greater cognitive deterioration than in those who were abstinent ($F(1, 335)=3.905$, $p=0.049$), but the changes did not significantly differ between psychotic deterioration, maintenance and improvement groups ($F(2, 335)=2.553$,$p=0.079$). The Spearman correlation analysis showed that there was a positive association between changes in cognitive scores and changes in psychotic symptoms among both abstinent MA users ($p=0.036$) and total MA users ($p=0.032$).

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CONCLUSION: MA-associated psychosis may increase the risk of cognitive impairment. In addition, deterioration of psychotic symptoms may increase the severity of cognitive deterioration. These findings emphasize the impact of psychotic symptoms on cognitive function in those who use MA and highlight the need for intervention among this population.

PSYCHIATRY
#44

Prevalence of HIV-Associated Neurocognitive Disorder: A Systematic Review and Meta-Analysis

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BACKGROUND: HIV-associated neurocognitive disorder (HAND) is highly prevalent despite the widespread of highly active antiretroviral therapy (HAART). The prevalence of HAND reported by studies varies. The object of this study was to determine the prevalence of HAND and its subtypes among different HIV-infected population, and to explore the heterogeneity and potential risk factors.

METHODS: The prevalence of HAND, asymptomatic neurocognitive impairment (ANI), HIV-associated mild neurocognitive disorder (MND), and HIV-associated dementia (HAD) by different diagnostic criteria, regions, demographic characteristics, treatment status, and HCV co-infectionstatus were pooled using random effects model and subgroup analysis.

RESULTS: A total of93 studies involving 21, 972 participants were included in the meta-analysis. The pooled prevalence rate of HAND was 45.1% (95% CI: 41.2-49.0), and the rate were 46.8%, 40.8% and 43.7% by 2007 Frascati criteria, GDS and IHDS, respectively. The pooled prevalence rate of ANI, MND and HAD by 2007 Frascati criteria were 25.3% (21.8-28.8), 13.7% (11.4-15.9) and 4.7% (3.8-5.6), respectively. The prevalence of HAND in South America was the highest (55.5%, 45.2-65.9), followed by Africa (50.0%, 36.6-63.5), and the latter had a markedly high rate of HAD (17.1%, 9.27-27.0). The prevalence of MND and HAD among antiretroviral-naive HIV-infected patients were 24.3% (0.0-59.4) and 16.6% (2.7-35.0), while rates among well-treated population were 11.2% (7.6-14.8) and 2.5% (1.4-3.7), respectively. The low CD4 cell count subgroups had higher rates of MND and HAD, while the low CD4 nadir subgroups had relatively higher rates of ANI. Populations with high proportion of HCV co-infection (>30%) had a significant higher prevalence of HAD (12.8%, 4.6-21.1), compared to the rates of lower co-infection groups (3.3%, 1.9-4.7; 1.5%, 0.2-2.8).

CONCLUSION: The prevalence rate of HAND can be affected by many factors. HIV-infected people should receive HAART in early stage to maintain a high level of CD4 cell count, and to prevent other opportunistic infections.

PSYCHIATRY
#45

Preventing Methamphetamine Seeking with a Memory Retrieval-Extinction Procedure

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BACKGROUND: It has been suggested that environmental cues associated with drug taking contribute to drug craving and relapse. In recent years, a memory retrieval-extinction procedure has been demonstrated to decrease reinstatement of cocaine, heroin and alcohol seeking in rats, and to reduce cue-induced drug craving in heroin and nicotine addicts. However, little is known about the neural circuitry mechanisms underlying this procedure. Here, we investigated the effect of memory retrieval-extinction procedure on methamphetamine relapse in rats and the underlying mechanisms.

METHODS: Firstly, we trained rats for methamphetamine self-administration and divided them into three groups: no retrieval + extinction, retrieval +1h delay + extinction, and retrieval + 6h delay + extinction, and assessed the effect of retrieval-extinction procedure on the priming-induced reinstatement, spontaneous recovery and renewal of methamphetamine seeking. Then we applied immunofluorescence and chemogenetic approaches to explore the neural mechanisms underlying the inhibitory effect of memory retrieval-extinction procedure on methamphetamine seeking.

RESULTS: We found that the memory retrieval-extinction procedure prevented the spontaneous recovery, renewal and priming-induced reinstatement of methamphetamine seeking. Significant activation of neurons in both prelimbic prefrontal cortex (PL) and infralimbic prefrontal cortex (IL) after CS retrieval was observed in CS-retrieval group compared with the no retrieval group. Moreover, chemogenetic inactivation of IL but not PL before CS retrieval blocked the inhibitory effect of retrieval-extinction procedure on methamphetamine seeking. In addition, labeling and reactivation of CS retrieval-extinction procedure-related neural ensembles in the IL successfully mimicked the effect of CS retrieval-extinction on methamphetamine seeking.

CONCLUSION: Our results indicated that the memory retrieval-extinction procedure is a promising effective method in preventing methamphetamine relapse, and IL activation may contribute to the disrupting effect of memory retrieval-extinction procedure on methamphetamine seeking.

PSYCHIATRY
#46

The Prevalence of Suicidal Thoughts and Attempts Among Medical Professionals: A Meta-Analysis and Systematic Review

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BACKGROUND: Medical professionals are at high risk for suicidal behaviors. However, the prevalence estimates of suicidal behaviors among medical personnels vary between studies. It is important to provide the overall prevalence estimates of suicidal behaviors for policy making in public health. This study aims to investigate the overall prevalence estimates of suicidal behaviors among medical professionals.

Poster Abstracts
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METHODS: A systematic search of Pubmed, Embase, and PsycINFO was used to identify relevant English-written studies published from January 1990 to January 2018. Prevalence estimates were pooled using random-effects meta-analyses. Heterogeneity was evaluated using the I2 statistic, and sensitivity analysis was performed to identify the sources for substantial heterogeneity. Subgroup analysis and meta-regression were conducted to study the effects of the potential variables. Publication bias was assessed using Begg's test.

RESULTS: A total of 5103 articles were identified, among which 62 longitudinal and cross-sectional studies were included in the analysis. The pooled overall estimates were 25.3%, 10.2%, and 6.9% for lifetime, 12-month and recent prevalence of suicidal thoughts. Lifetime and 12-month prevalence of suicidal attempts were 2.2% and 0.6%. The pooled prevalence was not influenced by screening instruments and demographics, except that the 12-month prevalence estimate of suicidal thoughts in females was higher than in males. Substantial heterogeneity was found in our study.

CONCLUSIONS: The prevalence of suicidal thoughts and attempts among medical professionals are high. It is of importance to develop and implement effective interventions to improve mental health of medical professionals.

PULMONARY
#47

Short-Term Exposure to High Ambient Air Pollution Aggravates Respiratory Symptom and Lung Function in Asthma Patients in Beijing, China

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BACKGROUND: Air pollution can cause acute exacerbation of asthma. We aimed to investigate the short-term respiratory effects of ambient air pollution in asthma patients in the context of high pollution levels in Asian cities.

METHODS: A panel of 32 asthma patients was recruited and repeatedly recorded for asthma control test (ACT) score , and measured for lung function in November 2015 - December 2016 . Daily ambient air pollution data including PM2.5, PM10, SO2, NO2 and CO were obtained from nearby central air-monitoring stations. Mixed effects models in R 3.3.2 were used to estimate the associations between exposures and health measurements with adjustment for potential confounders.

RESULTS: We collected repeated clinical data every 1 month for 2 to 13 times for 32 asthma patients (totally 266 visits). Interquartile range (IQR) increase in $PM_{2.5}$ (74.5 μg/m³, 6-d), PM10 (78 μg/m³, 5-d), SO2 (10 μg/m³, 7-d), NO2 (37 μg/m³, 6-d), CO (0.7 μg/m³, 6-d) were significantly associated with reduction in ACT score of 3.6 % (95% CI: -6.3%, -0.9%) , 2.8% (95% CI:-5.1%, -0.5%) , 3.2 % (95% CI: -5.5%, -0.9%), 3.8% (95% CI:-7.0%, -0.5%) and 2.9 % (95% CI: -4.3%, -1.4%), respectively. An IQR of 78μg/m³ in 7-d PM10 moving average concentrations were significantly associated with a 3.6% (95%CI: -5.6%, -1.5%) reduction in FEV1%.

CONCLUSIONS: Our results provide potential important public health implications that ambient air pollution may aggravate respiratory symptoms and lung function of asthma patients in Beijing, China.

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MEDICAL EDUCATION

#48

Training Pathways to Working as a General Practitioner in China

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BACKGROUND & OBJECTIVE: To achieve the goal of 300,000 general practitioners by 2020, an increase of 215,200 in a decade, China is utilizing multiple training pathways. To comprehensively illustrate general practitioner training strategies in China, this article illuminates these pathways.

METHODS: We used descriptive policy analysis. This involved taking an inventory of existing literature and source documents and developing a model to illustrate pathways for training general practice physicians.

RESULTS: The "rural doctor pathway" represents rural clinicians who had only basic training and practiced multiple years prior to training reforms. The "3+2" pathway to assistant general practitioner requires three years of junior college and two years of clinical training. The transfer pathway for current physicians requires one to two years of training. The "5+3" pathway comprises five years of Bachelor of Science degree training in clinical medicine and three years of standardized residency training. Despite the development of advanced degree programs their use remains limited.

CONCLUSIONS: These pathways illustrate significant heterogeneity in training of general practitioners. Training ranges from a two-year technical degree to a doctorate with research. Emphasis on the 5+3 track shows promise for China's goals of improved quality and 500,000 additional general practitioners by 2030.

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