



Michigan Medicine - PKUHSC 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

JOINT INSTITUTE

for Translational and Clinical Research



Annual Report 2018

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Table of Contents



PKUHSC Vice President Ning Zhang (right) tours the Michigan Medicine campus during the 2018 Joint Institute Symposium.

Letter from the Directors	2
Leadership	3
About the JI	4
Vital Statistics	5
New Projects for 2018	6-9
Project Profile: Deploying portable sequencing at the bedside	8
2018 Publications	10-12
Publication Focus: Air pollution and cardiovascular function	10
Extramural Funding	13
PKUHSC named National Center for International Research	14
2018 JI Symposium	15-17
Scholarly Exchange	18-19
New Dual Bioinformatics Degree Program	20
Other 2018 News	21

Letter from the Directors

Dear Colleagues,

We are pleased to present the 2018 Annual Report for the Michigan Medicine-Peking University Health Science Center Joint Institute (JI) for Translational and Clinical Research. This marks the first year that the JI has issued such a report – a testament not only an extremely productive 2018, but also to the fact that the breadth and depth of our partnership continues to grow.

Within these pages, find an accounting of our success – both since our 2010 launch and specifically in 2018. With nearly 50 funded projects to date (including 10 new awards for 2018), we believe the JI has come into its own as a model of international collaboration. These projects, each led by co-PIs from our respective institutions, touch on a growing number of disciplines, from cardiology and renal medicine to cancer research and emergency medicine.

All of this means that a growing number of individual collaborators are engaged in work through the JI, whether on shared research, administrative support through our unique research infrastructure cores, or in scholarly exchange opportunities. In 2018, our institutions welcomed a number of students and post-graduate learners for bi-lateral exchange. We also formalized plans to launch a new dual master's degree program in Bioinformatics which, starting in 2019, will further increase the number of learners traveling back and forth.

That exchange is important. Just as the discoveries forged by our research collaborations will improve care for patients, the meaningful relationships formed as our learners and faculty work alongside one another help us all gain new perspectives, insights, and appreciations. As physicians and medical educators, we understand the need to reach out beyond our own institutions – and beyond our own borders – for solutions to increasingly complex global healthcare challenges.

These challenges call for collaborations like the JI, which bring together some of the best minds in the world to tackle problems that disregard borders and transcend language, culture, and politics.

Xièxiè,



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Leadership



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About the JI

History

In 2010, Michigan Medicine, the academic medical center of the University of Michigan, and Peking University Health Science Center (PKUHSC) established the Joint Institute for Translational & Clinical Research, commonly known as the JI. Michigan Medicine and PKUHSC each contributed an initial \$7 million and both renewed their financial commitment with repeat \$7 million investments in 2015.

The JI was established to benefit both partner institutions by:

- enhancing translational research capacity;
- bolstering a qualified workforce in both basic science and clinical research;
- promoting student and faculty exchange; and
- helping faculty successfully compete for extramural funding.

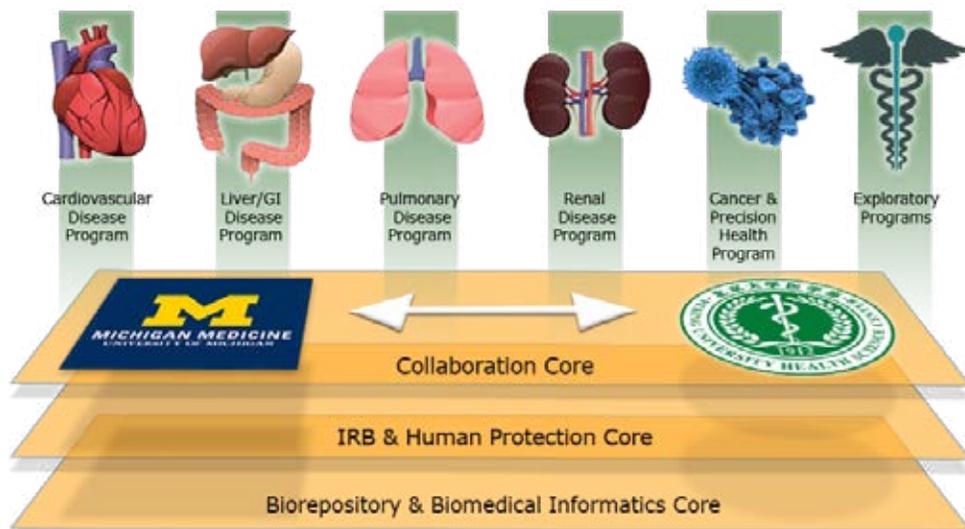
The JI allows faculty at both institutions to partner on research that neither side could conduct alone, advancing health for populations across both the US and China, and beyond.



Michigan Medicine faculty in Beijing for the 2017 Joint Institute Symposium.

Programs & Cores

Much of the research focuses on four key Program 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. In 2017, leaders designated two new areas for future project investment and focus: cancer research and precision health.



The JI's collaborative model of mutually agreed-upon research-area programs supported by supportive administrative cores makes it a unique academic institutional partnership.



By the Numbers

Vital Statistics To Date



JI Awards



Completed Projects



Patients Enrolled in Studies



Publications

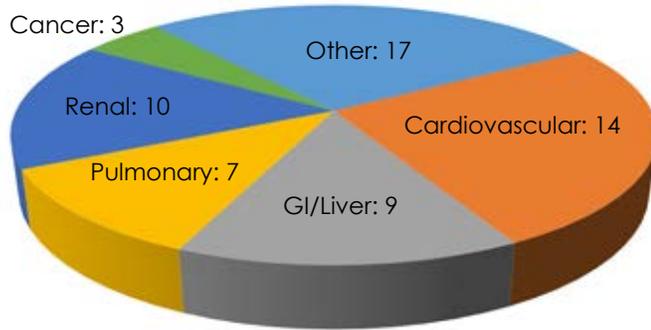


Extramural Funding

Research Areas

The JI fosters scientific research across many disciplines. At the outset, cardiovascular, renal, pulmonary, and gastrointestinal/liver medicine were prioritized. Over the years, other disciplines have been added. Most recently, JI leaders decided to prioritize research in the areas of cancer treatment and precision health. To date, 60 projects have received funding from nearly 200 submitted proposals.

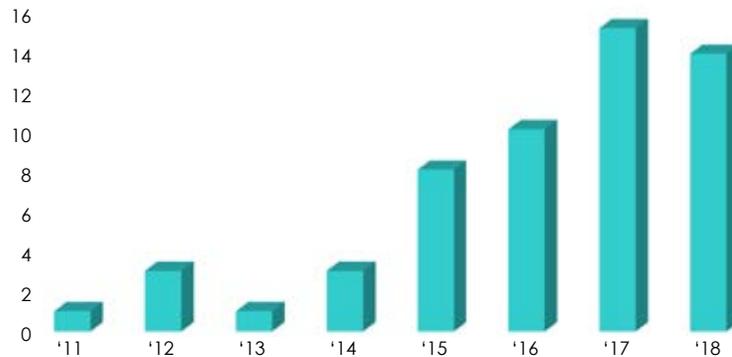
Awards by Program Area (2011-2019)



Publications

JI research has produced 67 publications to date, each co-authored by the respective PIs from each institution. JI research has appeared in leading academic medical journals including *Academic Medicine*, *PLoS ONE*, *Gastroenterology*, and many others.

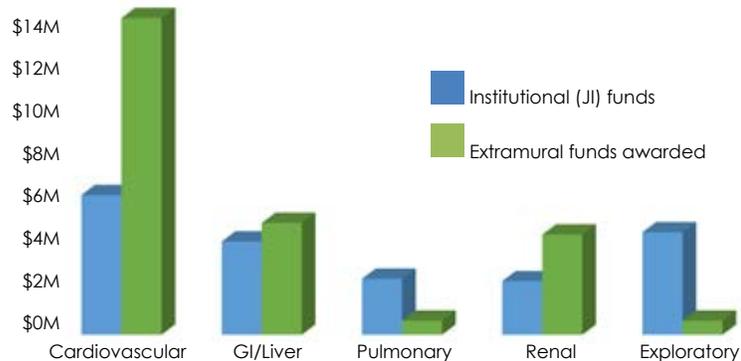
JI Publications (2011-2018)



Funding

Institutional investments made through the JI are intended to seed pilot projects that can ultimately garner extramural funding. To date, JI teams have received \$24 million in extramural funding for research as a result of their collaborations. Cardiovascular medicine research alone has resulted in \$14 million in extramural funding. Teams in GI/Liver, Renal, and Pulmonary medicine programs have garnered extramural funding as well.

Institutional & Extramural Funding (2011-2019)



New Awards for 2018

Ten new research projects have been selected for the most recent round of funding through the University of Michigan Health System's Joint Institute partnership with Peking University Health Science Center. The projects, each headed by a UMMS faculty member and their PKUHSC partner, span a number of areas, from exploring the genetic causes of intellectual disabilities to studying whether and how risk complications from diabetes differ between the U.S. and Chinese patient populations.



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 potentially tumoricidal TCR-T lymphocytes to treat HCC patients.

Co-Investigators



Clifford Cho, MD, FACS
UMMS



Yuan Hong, MD, PhD
PKUHSC

Therapeutic Implications of Natural Killer Cell Immune Surveillance in Lung Cancer

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 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. The study seeks to 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.

Co-Investigators



Venkateshwar
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UMMS



Jun Wang, MD, PhD
PKUHSC

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

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. The long-term objective of this proposal is to accelerate the identification and quantification of pathogens in VAP using novel, real-time molecular technologies. We will develop a protocol and pipeline that will rapidly identify respiratory pathogens in four hours via real-time metagenomics. In addition, we will develop a protocol and determine reference ranges that will rapidly quantify respiratory pathogens in two hours using a novel ultrasensitive PCR platform.

Co-Investigators



Robert Dickson, MD
UMMS



Ning Shen, MD
PKUHSC



New Awards for 2018

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, crusted 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 UMHS 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.

Co-Investigators



Lam Tsoi, PhD
UMMS



Trilokraj Tejasvi, MBBS, MD
UMMS



Yang Wang, MD
PKUHSC

β -adrenergic Receptor Activation in Cardiac Injury and Atherosclerotic Plaque Stability: Role of NADPH 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 how 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. 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.

Co-Investigators



Marschall Runge, MD, PhD
UMMS



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PKUHSC

Targeting Tumor Neoantigen-specific Tumor Infiltrating Lymphocytes in Nonsmall 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.

Co-Investigators



Andrew Chang, MD
UMMS



Jixian Liu, MD
PKU Shenzhen Hospital



New Awards for 2018

Investigators 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 and hope to identify mechanism-based therapies for the treatment of diabetes complications so treatment can be individualized and targeted appropriately.

Co-Investigators



Rodica Pop-Busui, PhD
UMMS



Luxia Zhang, MD, MPH
PKUHSC

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

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 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 venoaerterial ECMO for cardiogenic shock either in the setting of acute cardiac decompensation or failure to wean from cardiopulmonary bypass after cardiac surgery.

Co-Investigators

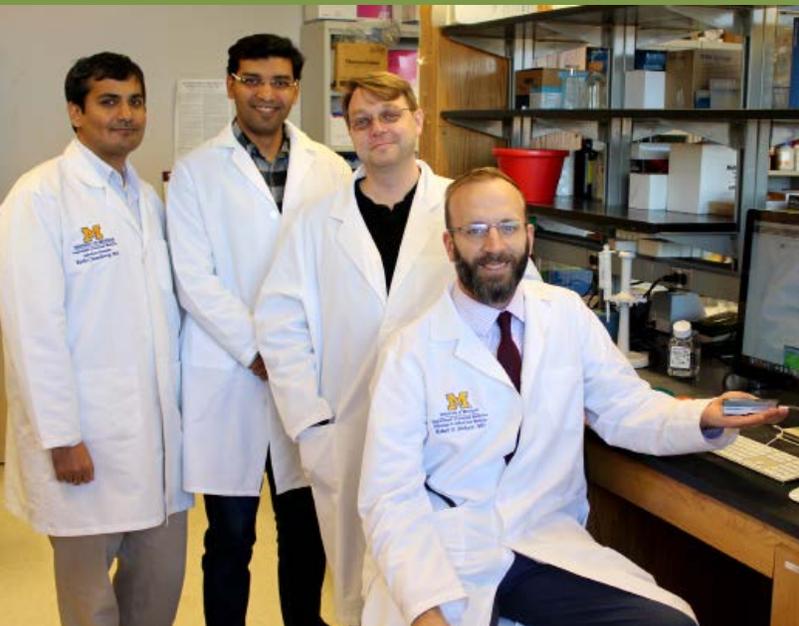


Paul Tang, MD, PhD
UMMS



Feng Wan, MD
PKUHSC

New Project Profile: Deploying portable sequencing bedside



Robert Dickson (right) and his Ann Arbor lab team.

While advances in genetics have revolutionized things like cancer treatment, the impact has not been universal across all areas of medicine.

Tumors can be biopsied and sequenced to help determine their cause at the molecular level and perhaps point to a targeted treatment. At the same time, the principal science used to identify and treat many common illnesses has remained essentially unchanged for more than a century.

“When we suspect a patient has a bacterial infection, we take a culture, give it time and see what grows – Louis Pasteur would totally recognize what we’re doing,” said Assistant Professor of Internal Medicine Robert Dickson. “Sequencing technology has revolutionized the way we think of microbiology in the body, but it hasn’t reached the bedside when it comes to diagnosing infections.”

Dickson’s latest project, a Joint Institute collaboration with Peking University Third Hospital Chief of Respiratory Medicine Ning Shen, aims



New Awards for 2018

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. Building on prior collaborations, we aim to identify and further study genetic causes of ID/DD&HLD patients. Establishing neuronal cell lines for promising candidate gene variants will provide a cellular platform for pathogenesis studies and in-vitro drug screens.

Co-Investigators



Margit Burmeister, PhD
UMMS



Jingmin Wang, PhD
PKUHSC

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

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. 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.

Co-Investigators



Yongqun He, PhD, DVM
UMMS



Jianmin Wu, PhD
PKUHSC

to change that. They plan to use new portable DNA sequencers to diagnose ventilator-associated pneumonia (VAP) in critical care patients – faster and more accurately than traditional culture tests are able to do. If successful, it could mean shorter detection times for VAP and also a reduced reliance on the kind of broad-spectrum antibiotics that contribute to drug-resistant bacteria. A major concern in every critical care unit, VAP occurs in between 10 and 40 percent of patients who remain on mechanical ventilation longer than two days, with individual risk increasing with each day a patient remains on the ventilator.

A primary method of VAP diagnosis is to sample the patient's lung using bacterial culture, a process that typically takes between 24 and 72 hours. Dickson believes they can reduce that time drastically through real-time sequencing using a new palm-sized nanopore sequencer, the MinION, that is powered by USB and ports into a laptop or desktop computer. Developed in the UK, the \$1,000 devices are about two thirds the size of a chalkboard eraser.

In their new study, Dickson and Shen plan to collect and sequence samples from the lungs of about 200 patients on ventilators across both institutions, comparing the speed and accuracy of the culture-test method to the mini sequencers.

“Our goal is to provide clinicians with rapid, reliable information regarding which antibiotics to prescribe, or even whether to prescribe them at all,” Dickson said. “This is a particularly good project for international collaboration because antimicrobial resistance is just as much a problem in Beijing as it is in Ann Arbor. This project is a real opportunity to tackle an important clinical concern with exciting new technologies.”



The portable sequencers being used in the study are about the size of a chalkboard eraser.



2018 Research Publications

JI collaborations resulted in a dozen publications in 2018, scholarship that appeared across a variety of disciplines in high-ranking journals such as *PLoS One*, *The American Journal of Cardiology*, and more.

Project: Dysfunctional HDL and Cardiovascular Disease (2011)

PIs: Eugene Chen (UMMS) & Guisong Wang (PKUHSC)

Program: Cardiovascular

Wang, G., Mathew, A. V., Yu, H., Li, L., He, L., Gao, W., . . . Pennathur, S. (2018). Myeloperoxidase mediated HDL oxidation and HDL proteome changes do not contribute to dysfunctional HDL in Chinese subjects with coronary artery disease. *Plos One*, 13(3).



Project: Particulate matter air pollution and high density lipoprotein dysfunction (2013)

PIs: Robert Brook (UMMS) & Jianping Li (PKUHSC)

Program: Cardiovascular

Huang, W., Wang, L., Li, J., Liu, M., Xu, H., Liu, S., . . . Brook, R. D. (2018). Short-Term Blood Pressure Responses to Ambient Fine Particulate Matter Exposures at the Extremes of Global Air Pollution Concentrations. *American Journal of Hypertension*, 31(5), 590-599.



Project: Particulate matter air pollution and high density lipoprotein dysfunction (2013)

PIs: Robert Brook (UMMS) & Jianping Li (PKUHSC)

Program: Cardiovascular

Mathew, A. V., Yu, J., Guo, Y., Byun, J., Chen, Y. E., Wang, L., . . . Brook, R. D. (2018). Effect of Ambient Fine Particulate Matter Air Pollution and Colder Outdoor Temperatures on High-Density Lipoprotein Function. *The American Journal of Cardiology*, 122(4), 565-570.



Publication Focus: Air pollution and cardiovascular function



Short-term exposure to high levels of air pollution can cause elevated blood pressure even in healthy adults, according to a newly published paper by Joint Institute researchers.

Michigan Medicine Professor of Cardiology Robert Brook and his collaborator, Research Professor Wei Huang at the PKUHSC School of Public Health, have been studying how air pollution impacts cardiovascular function in both Beijing and Ann Arbor. Their April 2018 publication in the *American Journal of Hypertension* marked the first research of its kind to harmonize studies of healthy people in Beijing, where air pollution levels are typically high, against counterparts in southeast Michigan, with comparatively clean air.

JI researchers Robert Brook, UMMS Professor of Cardiology (right), and UMMS Research Associate Robert Bard (left) visit the lab of Wei Huang, Peking University Professor of Public Health.

2018 Research Publications

Project: Molecular mechanisms of fibrosis and the progression from paroxysmal to persistent atrial fibrillation (2013)

PIs: Jose Jalife (UMMS) & Xuebin Li (PKUHSC)

Program: Cardiovascular

Takemoto, Y., Slough, D. P., Meinke, G., Katnik, C., Graziano, Z. A., Chidipi, B., . . . Noujaim, S. F. (2018). Structural basis for the antiarrhythmic blockade of a potassium channel with a small molecule. *The FASEB Journal*, 32(4), 1778-1793.



Project: Quantitative measurements of brain iron overload after intracerebral hemorrhage (2013)

PIs: Guoha Xi (UMMS) & Yinig Huang (PKUHSC)

Program: Cardiovascular

Liu, R., Li, H., Hua, Y., Keep, R. F., Xiao, J., Xi, G., & Huang, Y. (2018). Early Hemolysis Within Human Intracerebral Hematomas: An MRI Study. *Translational Stroke Research*, 10(1), 52-56.



Cao, S., Hua, Y., Keep, R.F., Chaudhary, N., and Xi, G. (2018) Minocycline effects on intracerebral hemorrhage-induced iron overload in aged rats: brain iron quantification with MRI. *Stroke*, 49 (4), 995-1002.



Project: Comparison of Chronic Kidney Disease (CKD) Prevalence, Risk Factors and Outcomes between China and the United States (2014)

PIs: Jennifer Bragg-Gresham (UMMS) & Luxia Zhang (PKUHSC)

Program: Renal

Wang, J., Wang, F., Saran, R., He, Z., Zhao, M., Li, Y., . . . Bragg-Gresham, J. (2018). Mortality risk of chronic kidney disease: A comparison between the adult populations in urban China and the United States. *Plos One*, 13(3).



"We've done international studies before and seen blood pressure-raising effects of air pollution in both Beijing and in Ann Arbor, but they were done with participants who are already at higher risk factors for cardiovascular disease," said Brook, MD. "We'd never really done a comparative study with completely healthy people like this."

Participants wore a small device to monitor air pollution levels for a 24-hour period before reporting to the clinic, where researchers took their blood pressure and gathered other biometric information. They repeated this process multiple times. The air quality data from their wearable monitors, supplemented with regional monitors in both locations, allowed the researchers to see if and how exposure to varying levels of pollution impacted blood pressure. In Michigan, there was no appreciable impact. Not so in Beijing, where the outdoor air pollution levels during the testing period were higher by factor of nearly 10.

"While modest at the individual level, the cumulative increase translates to a very large public health risk."

Robert Brook, MD
UMMS Professor of Cardiology

"Even if you're a healthy person living in Beijing, the pollution will still impact your blood pressure. The effect is typical of what we would expect to see if someone's weight changed by five or ten pounds," said Brook. "That kind of increase, while relatively modest at the individual level, cumulatively translates to a very large public health risk when you extrapolate across a city like Beijing of more than 20 million people."

Research Publications

Project: Genomic Evolution and Mutational Signature of Esophageal Cancer in Anyang, China (2014)

PIs: Jun Li (UMMS) & Yang Ki (PKUHSC)

Program: GI/Liver

Li, J., Yan, S., Liu, Z., Zhou, Y., Pan, Y., Yuan, W., . . . Ke, Y. (2017). Multiregional Sequencing Reveals Genomic Alterations and Clonal Dynamics in Primary Malignant Melanoma of the Esophagus. *Cancer Research*, 78(2), 338-347.

< **Cancer Research**

Project: DNA Methylation Changes Induced by Air Pollution Contributes to Chronic Airway Inflammation and Airway Remodeling in Moderate-to-Severe Uncontrolled Asthma (2014)

PIs: Steven Huang (UMMS) & Yahong Chen (PKUHSC)

Program: Pulmonary

Tripathi, P., Deng, F., Scruggs, A. M., Chen, Y., & Huang, S. K. (2018). Variation in doses and duration of particulate matter exposure in bronchial epithelial cells results in upregulation of different genes associated with airway disorders. *Toxicology in Vitro*, 51, 95-105.



Project: Targeting Peptidylarginine Deiminase (PAD) for Diagnosis and Treatment of Severe Inflammation (2015)

PIs: Hasan Alam (UMMS) & Baoguo Jiang (PKUHSC)

Program: Exploratory (Surgery)

Liang, Y., Pan, B., Alam, H. B., Deng, Q., Wang, Y., Chen, E., . . . Li, Y. (2018). Inhibition of peptidylarginine deiminase alleviates LPS-induced pulmonary dysfunction and improves survival in a mouse model of lethal endotoxemia. *European Journal of Pharmacology*, 833, 432-440.



Project: Prevention of Kidney Failure in Alport Syndrome by Application of Podometric Technology (2015)

PIs: Roger Wiggins (UMMS) & Jie Ding (PKUHSC)

Program: Renal

Li, B., Zhang, Y., Wang, F., Nair, V., Ding, F., Xiao, H., . . . Ding, J. (2018). Urinary epidermal growth factor as a prognostic marker for the progression of Alport syndrome in children. *Pediatric Nephrology*, 33(10), 1731-1739.

< **Pediatric Nephrology**

Project: Identification of Shared and Specific Marker Panels for Diabetic Kidney Disease Progression (2016)

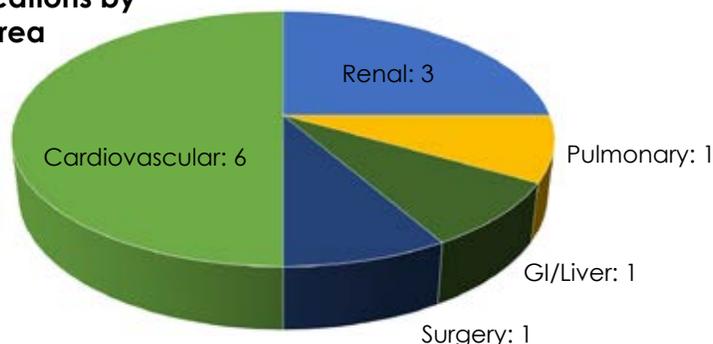
PIs: Wenjun Ju (UMMS) & Ming Chen (PKUHSC)

Program: Renal

Wu, L., Li, X., Chang, D., Zhang, H., Li, J., Wu, S., . . . Zhao, M. (2018). Associations of urinary epidermal growth factor and monocyte chemotactic protein-1 with kidney involvement in patients with diabetic kidney disease. *Nephrology Dialysis Transplantation*.



2018 Publications by Program Area





2018 Extramural Funding

As JI collaborations mature, researchers have increasingly been able to leverage their JI work to garner extramural funding to expand their efforts far beyond what the initial pilot project funding allowed. To date, nine JI collaborations have generated 12 grants worth more than \$17 million in extramural funding. That's a little more than the \$14 million invested (of \$28 million allocated) to date on JI projects collectively from both institutions.

Most (though not all) of that extramural funding to date has come from the National Institutes of Health for studies in cardiology, pulmonary medicine, renal medicine, and more. In 2018 alone, UMMS researchers were awarded two new NIH grants (R01 and U01) worth more than \$6 million.

Extramural Funds Secured in 2018 for Further Research in Hepatology, Cardiovascular Medicine



Anna Lok



Thomas Wang

Novel Strategies to Improve Liver Cancer Surveillance Uptake and Early Detection

Total Funding: \$3.39 million (NIH)

Anna Lok, MD
Assistant Dean for Clinical Research
Thomas Wang, PhD, MD
Professor of Biomedical Engineering



Eugene Chen



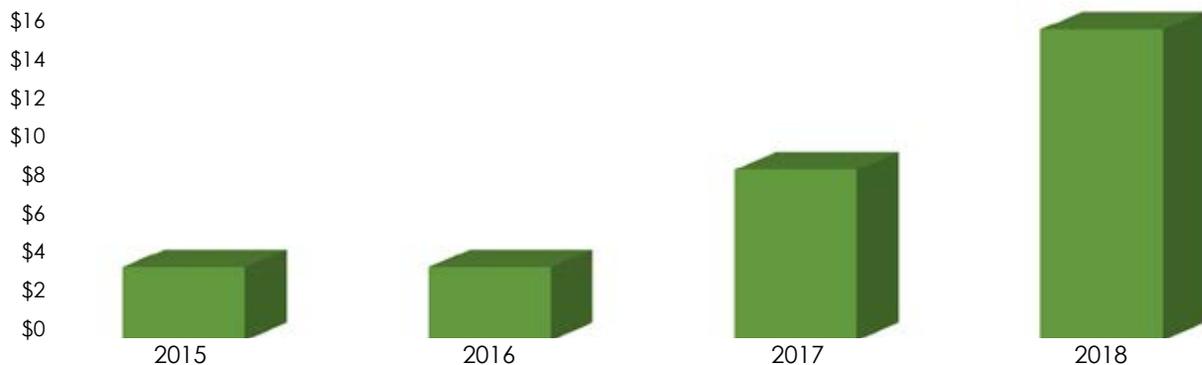
Subramaniam Pennathur

KLF14 and Atherosclerosis

Total Funding: \$2.82 million (NIH)

Yuqing Eugene Chen, MD, PhD
Professor of Cardiovascular Medicine
Subramaniam Pennathur, MD
Professor of Nephrology

Cumulative Extramural Funding (2015-2018)



Feature

China recognizes PKUHSC for international research



Leaders from PKUHSC and invited international collaborators including JI Co-director Joseph Kolars (center) in Beijing for a National Center celebration.

PKUHSC was recently recognized by the Chinese government as a National Center for International Research.

The school is the first academic medical center to receive the honor, bestowed early this year from the Chinese Ministry of Science and Technology. While PKUHSC has many partnerships abroad, the relationship with Michigan Medicine is the institution's longest-running and largest international partnership.

University of Michigan leaders including JI Co-director Joseph Kolars visited the PKUHSC campus in January for a celebration to dedicate the new National Center.

"On behalf of Michigan Medicine, we treasure our friendship with Peking University Health Science Center and are extremely proud to celebrate this achievement with them," said Kolars, UMMS Senior Associate Dean for Education and Global Initiatives. "This National Center designation is well deserved and will no doubt help highlight and elevate the work of our JI researchers."

During the celebration event, several JI project investigators from PKUHSC were able to present about their collaborations with Michigan Medicine colleagues to an audience that included top-level officials from the Chinese Ministry of Science and Technology.

"This National Center designation distinguishes our collaboration and will be beneficial in helping to leverage more government support for our partnership and joint projects," said PKUHSC Vice President Ning Zhang.

"The National Center designation is well deserved and will no doubt serve to highlight and elevate the work of our JI researchers."

- Joseph Kolars, MD
UMMS Sr. Associate Dean for
Education & Global Initiatives



PKUHSC is the first academic medical center to be singled out by the Chinese Ministry of Science and Technology for a National Center designation.

2018 Symposium



Attendees gather for a group picture during the 2018 JI Symposium on the Michigan Medicine campus, the largest JI Symposium yet.

Nearly 100 of China's top physician researchers visited Ann Arbor in October for the eighth annual Joint Institute Symposium, the largest meeting yet between Michigan Medicine and PKUHSC.

The three-day Symposium included sessions on cancer research, medical education, addiction, dental health, and more, as well as time for individual collaborators to advance ongoing projects.

Since its launch in 2010, the JI has funded nearly 50 projects and the annual symposium has grown from a few dozen participants to hundreds of attendees representing many disciplines between the partner institutions.

"I am enthusiastic about the research programs I've seen at UMMS and excited about the JI partnership. While we have many international partnerships, the JI is our top priority."

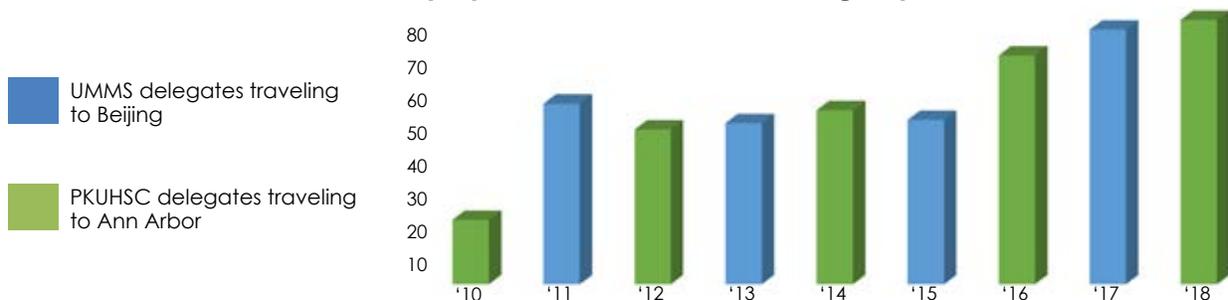
- Ning Zhang, PhD
PKUHSC Vice President

"It's gratifying to think about how far we've come. In eight short years, the JI has become a model for how institutions can sustain meaningful collaborations through common goals, shared values, and mutual respect," said JI Co-director Joseph Kolars, UMMS Senior Associate Dean for Education and Global Initiatives.

Kolars co-directs the JI with PKUHSC Vice President Ning Zhang, PhD, a Johns Hopkins-trained molecular biologist who recently joined the faculty at PKUHSC. The 2018 symposium marked Zhang's first.

"I am very enthusiastic about the research programs I've seen here (at UMMS) and excited about the JI partnership. While we have many international partnerships, the JI is our top priority," he said. "We've never organized a program like it with any school before. Our leadership is engaged. More important, our faculty are very excited about this collaboration."

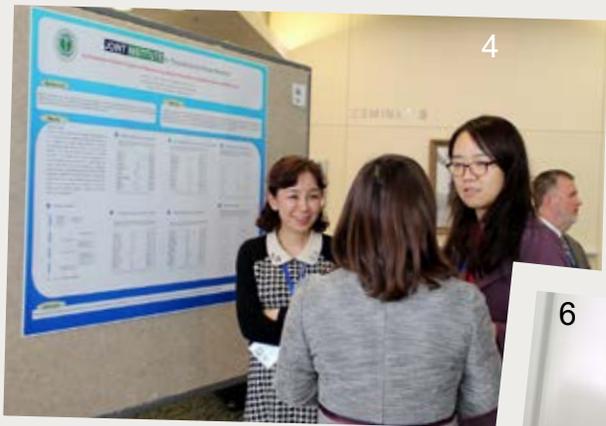
Symposium attendees traveling to partner institution



Symposium Scrapbook



2018 Meeting Pictures



4



5



6



8



7

1. PKUHSC Professor of Critical Care and Pulmonary Medicine Yahong Chen presents research at the poster session.
2. JI Co-director Joseph Kolars, UMMS Sr. Associate Dean of Education & Global Initiatives, greets Symposium attendees.
3. Rogel Cancer Center Director Eric Fearon talks with PKUHSC Vice President and JI Co-director Ning Zhang.
4. PKU National Institute for Drug Dependence researcher Shiqiu Meng (right) and her colleague Jie Shie discusses their JI project.
5. U-M President Mark Schlissel delivers opening remarks to Symposium attendees.
6. Student volunteers greet attendees at the registration table.
7. PKUHSC President Qimin Zhan participates in an interview with a Chinese film crew.
8. UMMS Executive Vice Dean for Academic Affairs Carol Bradford asks a question during a presentation.
9. The Symposium banquet featured a traditional Chinese music performance.
10. UMMS Dean and Michigan Medicine Executive Vice President for Medical Affairs Marschall Runge welcomes Symposium attendees.
11. Visitors tour the North Campus Research Complex.
12. A Symposium panel discussion on precision health and cancer treatment.



Scholarly Exchange

UMMS resident enjoys clinical, research rotation at PKUHSC



UMMS Pediatrics-Internal Medicine Resident Mark Kluk (center, left) with colleagues at Peking University First Hospital's Pediatrics.

One UMMS resident's 2018 rotation in China included clinical work plus a little something extra that could help shape how visitors to UMMS are received.

Pediatrics-Internal Medicine resident Mark Kluk spent the month of March at Peking University First Hospital, where he launched a research project that seeks to understand how Chinese medical students and post-graduate learners perceive the value of international educational experiences.

"The basic idea was to delve deep into their perceptions on the value of these rotations. In our own medical education culture, we value it highly. It's a popular thing to do. I wanted to see how they felt about it because there is a significant difference in the culture around medical education," said Kluk, MD, MPH.

The Michigan Medicine pediatrics department has increasingly been creating opportunities for residents to engage in global health work overseas. Kluk is the first Pediatric resident to visit China and First Hospital. His research project, conducted with First Hospital pediatrician Jianguang Qi, may help advance educational exchange programs between PKUHSC and UMMS.

"In addition to clinical work, I wanted to do something academic that would be meaningful and potentially useful to both institutions long after my short visit was over," Kluk said. "With the information we gathered, we're hoping to begin shaping a curriculum for visiting international students and residents."

Kluk was able to survey nearly 60 residents and students during his visit. The vast majority were interested in some sort of international rotation, preferably in the United States or Canada. They are primarily interested in clinical rotations (versus research or didactic-focused experiences), and are most attracted to specialty or sub-specialty rotations (as opposed to general pediatric rotations).

"I got much more out of it than I was expecting, and that has to do with selecting a site where U-M has an ongoing partnership," Kluk said. "That is one of my biggest takeaways – when we host visiting residents here, we need to make sure we have a similar support system in place because it helps people have formative experiences."

Scholarly Exchange

Visiting PKUHSC physician spends year at Michigan Medicine



FanFang Wang (center) a Peking University Third Hospital cardiologist, with the Michigan Medicine nuclear cardiology team.

A Chinese physician spent all of 2018 at Michigan Medicine to learn nuclear cardiology techniques. FangFang Wang, MD, worked closely with Associate Professor of Radiology and Cardiovascular Medicine Venkatesh Murthy and others to learn techniques like myocardial perfusion imaging and positron emission tomography.

Such noninvasive imaging methods, which can measure blood flow through the heart and identify areas that have been damaged, are increasingly common in the United States but not yet widespread in China – although Wang is hoping to change that.

“Ann Arbor has been a very good place to study. The biggest thing that impressed me is how engaged everyone is in their work and how happy they are to teach and share their skills.”

- FangFang Wang, MD
PKU Third Hospital Cardiologist

“We typically rely on other methods that are more limited and don’t always provide as much information,” she said. “I’ve learned a lot very quickly here because the nuclear cardiology program is so well developed.”

Wang first visited Ann Arbor as an attendee of the 2014 Joint Institute Symposium. Her 2018 return to Michigan Medicine, funded by the Chinese government, marked her first extended visit.

“Dr. Wang is a really wonderful addition to our team. Her participation has allowed us to learn more about cardiology in China, including how the challenges they face are both similar and different,” said Murthy, MD. “She’s also been a major help to our research programs and has been really wonderful to discuss clinical cases with.”

In addition to expanding her clinical skills, Wang also engaged in nuclear imaging research with Murthy and other Michigan Medicine collaborators exploring ischemia and inflammatory heart disease.

“Ann Arbor has been a very good place to study. The biggest thing that has impressed me is how engaged everyone is in their work and how happy they are to teach and share their skills,” Wang said. “Their focus and enthusiasm makes you love your job.”

Feature

UMMS, PKUHSC to launch a dual bioinformatics degree



From left, Yuxin Yin, MD, PhD, Dean of Basic Medical Sciences; Ming Xu, PhD, Executive Deputy Dean of the Graduate School; and Ying Yang, MD, Deputy Director of the Residency Education Office, all visited UMMS in May to discuss the launch of a new dual degree program in Bioinformatics.

Leaders from UMMS and PKUHSC in 2018 agreed to launch a new dual degree in bioinformatics. The program will bring top graduate students from China to Ann Arbor starting in the fall of 2019.

Participants will split their time between Ann Arbor and the PKUHSC campus in Beijing, earning a master's degree from each institution. The initiative marks a meaningful expansion of the ongoing partnership between the two medical schools.

"This is taking a successful research platform and adding an education component, which will only serve to make the partnership stronger," said UMMS Professor of Bioinformatics Margit Burmeister, PhD, who has long had partnerships in China and is helping to shape the new dual degree program.

"Big data is a good area to focus on because it is such a growth field. In China, they have strong traditional disciplines – medicine, engineering, computer science. But bioinformatics is about putting those individual disciplines together into a meaningful degree program, something we at U-M have a lot of experience in," Burmeister said.

A leadership group from PKUHSC visited Ann Arbor in May 2018 to work through the program details. UMMS is set to take 4-5 students the first year, with an opportunity for program expansion down the road.

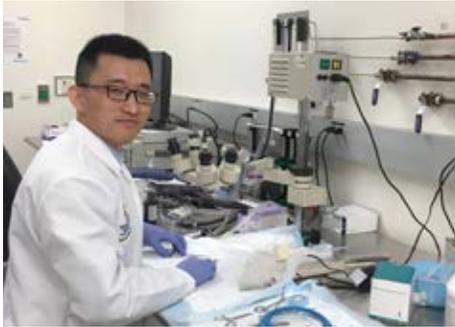
Bioinformatics uses computers to sort, analyze, and interpret the huge genomic datasets that are increasingly prevalent in precision healthcare. UMMS has one of the United States' largest and most well established bioinformatics programs. PKUHSC recently launched its own.

"Bioinformatics is growing so fast in China that many students want a master's and then they want to begin their career. If a student is able to get a degree from both PKUHSC and UM, that will set them apart," said Yuxin Yin, MD, PhD, Dean of Basic Sciences and Director of the Institute of Systems Biomedicine at PKUHSC. "There is a lot of interest in this program among our students."

"Bioinformatics is growing fast in China. If a student is able to get a degree from both PKUHSC and UM, that will set them apart."

*- Yuxin Yin, MD, PhD
Dean of Basic Science
Director of the Institute of
Systems Biomedicine, PKUHSC*

Other 2018 News



Jing Zhou at UMMS

A 2018 Call for Proposals received a record 33 letter of intent responses from faculty interested in launching new JI research projects.

PKU Third Hospital Cardiologist FangFang Wang, MD, spent nearly all of 2018 as a visiting scholar at Michigan Medicine to learn nuclear cardiology imaging techniques.

Michigan Medicine Pediatrics Resident Mark Kluk completed a month-long clinical rotation in Peking University First Hospital's pediatrics unit in March.

PKU Second Hospital Attending Physician Jing Zhou, MD, spent much of 2018 as a visiting scholar in the lab of Michigan Medicine Professor of Surgery Hasan Alam, MBBS, conducting research for a JI project co-led by Alam and his PKUHSC counterpart, Baoguo Jiang, MD.



Opening the new Center for International Cooperation and Exchange at PKUHSC

UMMS Director of Asia 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 the National Medical Education Development Center at PKUHSC in May. 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 institution's Center for International Cooperation and Exchange in May.

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.

Michigan 10 new JI project awards included research in Cardiovascular, GI, Pulmonary, Renal, Pediatric, and Dermatology medicine.

UMMS Professor of Ob-Gyn and Urology John DeLancey visited Beijing in September to participate in the PKU Urogynecology and Cosmetic Gynecology conference.

The eighth annual JI Symposium took place in Ann Arbor and drew nearly 100 JI researchers, leaders and delegates from PKUHSC, the largest meeting yet between the two institutions.

JI Co-Director Joseph Kolars, University of Michigan Medical School Sr. Associate Dean for Education and Global Initiatives, visited PKU Shenzhen Hospital in November to explore future collaborations.

PKUHSC was designated as a National Center for International Research by the Chinese Ministry of Science and Technology, the first academic medical center in China to receive the distinction.



John DeLancey at PKU.



Joseph Kolars at PKU Shenzhen Hospital.

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