JI NEWS

Joint Institute Newsletter: September 2016

Upcoming Symposium update

JI featured in Academic Medicine

Beijing research projects lead to student publications

New JI project announcements

Resident’s PUHSC postcard

PUHSC collaboration garners Fulbright Award
Letter from the Directors

Dear colleagues:

As the Sixth Annual JI Symposium approaches, we couldn’t be more enthused about the opportunity to strengthen our partnerships, share recent successes, and celebrate new collaborations and projects. This edition of the newsletter previews the event, which is being hosted at the University of Michigan for the third time. Inside, find the schedule, as well as confirmed speakers and panel information.

Also find information about the newest JI research proposals to receive funding: eight projects that are sure to advance science and health in both China and the US. We’ll also examine a new PUHSC/U-M collaboration being funded by a prestigious Fulbright Distinguished Chair award – a project rooted in a meeting at the 2014 JI Symposium.

JI partnerships aren’t just about faculty; students and physicians-in-training benefit, too. Read about a U-M resident’s influential rotation with PUHSC, as well as several medical students who are now published authors after working in China under JI mentors.

Indeed, we have much to celebrate. Our institutional relationship continues to thrive to the benefit of our colleagues and students, to say nothing of the many future discoveries that will no doubt improve healthcare for people everywhere. Please enjoy this issue and we look forward to seeing many of you at this year’s JI Symposium.

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Sixth Annual Joint Institute Symposium update

Join us for the 2016 JI Symposium, to be held in Ann Arbor, MI Oct. 12-14, 2016. Top researchers and faculty from China’s Peking University Health Science Center (PUHSC) will be visiting the U-M campus for the event. Faculty and students engaged in global health work or interested in launching new partnerships are encouraged to attend. Visit www.puuma.org for more information.

Schedule of Events

**Wednesday, Oct. 12**

Break-out Group Meetings

Team Dinner

(invitation only)

**Thursday, Oct. 13**

Opening Ceremony

Qi-Min Zhan Keynote

Marschall Runge Keynote

Panel Discussion I

Poster Session

Panel Discussion II

JI Projects Report

Dinner Banquet

(invitation only)

**Friday, Oct. 14**

JI Program Concurrent Sessions

Panel Discussion III

Closing Ceremony

PUHSC Alumni Event

(invitation only)

Two keynote speakers

Dr. Marschall Runge
UMHS Executive Vice President for Medical Affairs & Dean of the Medical School

Dr. Qi-Min Zhan
PUHSC President

Three engaging panels

I. Cancer Genetics & Precision Oncology
moderated by:
PUHSC President Qi-Min Zhan, MD, PhD
UMMS Professor of Bioinformatics Gil Omenn, MD, PhD

II. Precision Medicine: New Frontiers and Challenges
moderated by:
PUHSC Prof. & Dean of Pharmaceutical Sciences Demin Zhou, PhD
UMMS Prof. & Chair of Learning & Health Sciences Chuck Friedman, PhD

III. Preparing for the Consequences of Precision Medicine
moderated by:
PUHSC School of Public Health Professor Yangfeng Wu, MD, PhD
UMMS Professor & Chair of Bioinformatics Brian Athey, PhD
Beijing research projects lead to publications for multiple students

Several medical students are now published authors following the completion of research projects under the guidance of U-M Hepatology Professor Anna Suk-Fong Lok, MD, and PUHSC’s Dr. Lai Wei.

The projects explored aspects of liver disease treatment and care and included extensive on-the-ground research in China. The resulting publications, in recent issues of Digestive Diseases & Sciences and Liver International, garnered author credits for four U-M Medical School students.

“It’s a great experience for the students and without the JI, it wouldn’t be possible,” said Dr. Lok. “My partners dedicated a lot of time and resources to these studies, from introducing the students to the clinics and obtaining IRB approval, to helping interpret results and reviewing manuscripts.”

Fourth-year U-M medical student Fanny Du visited China in the summer of 2014, helping survey hundreds of patients seen in liver disease clinics about their care experience. Those results were compared against data from patients seen in Ann Arbor liver clinics. The findings, A Comparative Study of Liver Disease Care in the USA and Urban and Rural China, have been published in Digestive Diseases and Sciences.

A second study, Survey of Hepatitis B Knowledge and Stigma among Chronically Infected Patients and Uninfected Persons in Beijing, appears in Liver International. Students Jiaxin Huang, Jeremy Balch and Mary Guan spent several weeks in Beijing in the summer of 2015 interviewing more than 1,200 people to study stigma around Hepatitis B.

“Given our findings, we believe that public health education can improve understanding of transmission of Hepatitis B and alleviate stigma toward the patients,” Ms. Huang said.
Prior to her Internal Medicine residency at PUHSC, U-M graduate Anum Minhas had never been to China and spoke no Chinese, which was part of the attraction of the residency.

“I wanted an experience that would be completely different both culturally and socially, one which would take me out of my comfort zone and broaden my horizons,” said Minhas, one of two UMMS graduates to do a rotation at PUHSC this year.

Minhas spent four weeks working alongside her PUHSC mentor, Dr. Xuebin Li, Professor and Chair of Cardiovascular Medicine at PUHSC Second Hospital. During her stay, she spent time in the cardiac critical care unit and the cardiac cath lab, as well as on general hospital rounds with Dr. Li. She was also able to observe patient care in a clinic offering traditional Chinese medicine, including acupuncture and cupping, a therapy which uses heated glass cups applied to the patient’s skin.

She was struck by the similarities in equipment and processes, as well as differences in organizational roles and responsibilities between the Chinese and US health systems.

“There were no internal medicine residents as everyone sub-specializes,” she said. “Most of the members, aside from the chief, are not involved in decision making, which was striking – in the US, residents are expected to make decisions and manage the team.

“It was also beneficial to learn from a hospital system that is very cost conscious,” she continued. “We don’t consider cost often as physicians in the US, but in China, doctors often discuss cost with their patients. It was eye opening to realize that resource allocation is so carefully considered elsewhere in the world.”
Doctor’s international collaboration garners rare Fulbright scholarship

A University of Michigan doctor is headed for China and U-M’s partner medical school this year after being named a 2016 Fulbright Distinguished Chair in Social Sciences.

Michael Fetters, a professor of Family Medicine, is the first U-M Medical School faculty member in recent memory to receive a Distinguished Chair honor, Fulbright’s rarest and most coveted award. He will spend five months in Beijing teaching and leading a joint research project with colleagues at Peking University Health Science Center (PUHSC), U-M’s partner school in the Joint Institute for Translational and Clinical Research.

“We are so proud of Dr. Fetters. This honor not only represents an amazing personal accomplishment for him, but will also be of great benefit to our partnership,” said Dr. Amy Huang, U-M Global REACH Director of China Programs. “Dr. Fetters’ Fulbright award demonstrates the value of fostering relationships between our U-M faculty and collaborators overseas, as both institutions stand to gain a great deal from this work.”

Sponsored by the US government, the Fulbright Scholarship Program is intended to connect US scholars with counterparts overseas in order to collaborate on global issues. While more than 1,200 scholars will lend their expertise abroad this year on Fulbright scholarships, only about 40 of those received Distinguished Chair awards, Fulbright’s top honor.

Dr. Fetters’ winning proposal will find him partnering with Dr. Yali Cong, PUHSC’s Dean of Medical Ethics. While candid diagnoses to patients are the norm in the United States, the same does not always hold true in China, where family members often play a larger role in making care and communication decisions.

Michael Fetters will spend five months at PUHSC studying cancer diagnosis communication.

While this may be changing, I believe that telling people they have cancer probably remains the exception rather than the rule in many parts of China,” said Dr. Fetters. “We shouldn’t make assumptions about what the right approach is, but our goal through this research would be to create more open public dialogue about approaches to involving patients and family members in treatment and care decisions.”

Dr. Fetters’ research will focus on Chinese physicians’ attitudes regarding cancer communication in both the diagnosis and treatment stages. The study has practical implications for Western researchers collaborating with colleagues in China as they navigate conflicting cultural standards between the two countries;
patients must consent to be involved in clinical research trials – and consent is difficult to obtain if the patient doesn’t understand their diagnosis.

“As we’re becoming more of a global economy, this kind of Fulbright scholarship allows us to understand each other better and also puts the University of Michigan and the Family Medicine department at the forefront of research that has a long-term impact in different parts of the world,” said Dr. Philip Zazove, MD, the George A. Dean, MD Chair of Family Medicine. “This is a well-deserved honor for Dr. Fetters and a testament to the department, the university and the research being done across U-M.”

Co-Director of the University of Michigan Mixed Methods Research and Scholarship Program, Dr. Fetters also will lend his expertise by teaching a graduate-level mixed methods research course at PUHSC. Dr. Fetters will be promoting mixed methods research in China by leading faculty seminars and workshops on mixed methods research at PUHSC and other Chinese institutions.

The Distinguished Chair award is Dr. Fetters’ second Fulbright scholarship. He spent time in Japan in 1992 on a different “Japan Today” Fulbright grant, when he explored cancer disclosure in that country. That early project set the stage for the rest of his scholarly career, Dr. Fetters said.

“Our research could help inform healthcare policy in China and the teaching of medical education and medical ethics,” he said.
Introducing the new

Congratulations to the following collaborators

**Shared and disease-specific genetic study among IgA nephropathy, henoch-schonlein purpara nephritis, and Iupus nephritis**

Celine Berthier, PhD, Assistant Research Scientist, Internal Medicine, UMMS
Hong Zhang, MD, PhD, Professor of Internal Medicine, PUHSC

Berthier and Zhang plan to build and validate a fine mapping of the genetic variant regions associated with IgAN, LN, HSPN, three types of glomerulonephritis prevalent in both China and the US. Their pilot will help customize patient care with disease- and patient-specific therapies that are less toxic.

**Building collaborations to address drug problems in the United States and China**

Frederic Blow, PhD, Professor of Psychiatry, UMMS
Lin Lu, MD, PhD, Director of National Inst. on Drug Dependence, PUHSC

The award will foster collaborations between top addiction researchers at U-M and PUHSC, starting with examinations of effective chronic pain treatment among patients diagnosed with HIV/AIDS.

**Identification of shared and specific marker panels for diabetic kidney disease progression**

Frank Brosius III, MD, Professor of Internal Medicine, UMMS
Min Chen, MD, PhD, Professor of Nephrology, PUHSC

Building on a successful 2013-15 JI study that identified a biomarker predictive of chronic kidney disease, the partners’ new project continues to explore biomarkers that could aid in the early diagnosis of chronic and diabetic kidney diseases.

**Understanding the role of potassium channel gene mutations in pediatric epilepsy**

Lori Isom, PhD, Professor of Pharmacology, UMMS
Yuwu Jiang, MD, PhD, Professor of Pediatrics, PUHSC

Isom and Jiang seek to understand the molecular basis of genetic epilepsy. Working together, they hope to discover novel epilepsy mutations in potassium channel genes in order to provide useful platforms for future drug discovery.
Defining molecular mechanisms and biomarkers for progressive renal end-stage organ damage in vasculitis

Matthias Kretzler, MD, Professor of Internal Medicine, UMMS
Minghui Zhao, MD, PhD, Professor of Medicine, PUHSC

Zhao has accumulated a prospective group of over 500 patients with Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), among the largest such cohorts in the world. Meanwhile, Kretzler has generated gene expression profiles from 89 patients with AAV. Integrating this work across continents will provide insight into renal AAV disease pathogenesis.

Image-guided surgery of hepatocellular carcinoma

Thomas Wang, MD, PhD, Professor of Internal Medicine, UMMS
Jiye Zhu, MD, Chief of Center for Transplantation, PUHSC

The new project will build upon six years of previous collaborative effort. Wang and Zhu study a peptide that could be useful in precision medicine treatments for certain hepatitis B-derived cancers, offering advantages for improved distribution in solid tumors including deeper penetration, greater extravasation, and faster diffusion.

Multi-ethnic study of genetic risk factors to discover mechanisms of aortic aneurysm and dissection

Cristen J. Willer, PhD, Assistant Professor of Internal Medicine, UMMS
Zhe Zhang, MD, Professor of Cardiac Surgery, PUHSC

The team aims to identify the underlying genetic causes of aortic aneurysm and dissection in multi-ethnic cohorts using exome sequencing and genome-wide association approaches. This study has the potential to provide paradigm-shifting discoveries for this devastating cardiovascular disease.

Human embryo mosaicism influence on Preimplantation Genetic Screening (PGS), embryo development, and human Embryonic Stem Cell (hESC) development and genetic stability

Gary D. Smith, PhD, Professor of Molecular & Integrative Physiology, UMMS
Jie Qiao, PhD, President and Chief Physician, PUHSC Third Hospital

The top infertility experts at PKU and U-M plan to question some common assumptions about pre-implantation genetic screening methods in order to improve infertility treatment and outcomes.
Cardiovascular Program

HDL: U-M IRB is already approved and blood collection is complete. Samples have not been analyzed for the new proposal pending IRB approval in PUHSC. Two papers are currently being written based on findings of the previous grant funding cycle.

Aortic Dissection: About one new patient is recruited each week. The PUHSC team has performed proteomics analysis on 15 dissection patients, 15 healthy control patients, and 15 acute coronary syndrome patients. New target protein biomarkers will be identified by the U-M and PUHSC team, and be verified in more patients’ blood samples.

High Density Lipoprotein Dysfunction: Both studies at PUHSC and U-M have been successfully completed. Initial results demonstrate adverse effects of air pollutants on several cardiovascular parameters in Beijing, particularly among overweight participants. The findings in Michigan thus far do not demonstrate consistent evidence of adverse health effects, likely due to the extremely low levels of air pollutants encountered during this time period. The team will finalize analyses in the coming months and aim to complete blood biomarker analyses related to HDL function this year.

Renal Program

CKD Comparison: The manuscript for Aims 1 & 2 (comparing both the prevalence of CKD and magnitude of association with risk factors between the US and China) is currently being edited after comments from AJKD. The team is discussing results from Aim 3 (assessing trends in risk factors and prevalence of CKD in the US to predict future burden of CKD in China), while the manuscript for Aim 4 (comparing mortality risk from markers of CKD between the countries) is currently being drafted. Dr. Jinwei Wang began his Fogarty Fellowship on Aug. 1 and will continue to explore these topics.

Alport Syndrome: To date, 168 urine samples have been analyzed. Preliminary data has been submitted for abstract presentation at the American Society of Nephrology conference this November in Chicago. Biopsy sample analysis has been implemented with an initial set of 16 biopsies processed in Beijing and images sent to Ann Arbor for analysis. The data obtained showed a strong correlation of podocyte density with 24-hour urine protein excretion (R²=0.44) as previously found in Ann Arbor samples. This result provides support for the concept that accelerated podocyte detachment is a key underlying mechanism driving progression in Alport syndrome, and can potentially be used as a clinical monitoring strategy. Ongoing studies are focused on establishing the reproducibility of the urine podocyte excretion rate values for any individual patient over time, and increasing the number of the biopsies analyzed over a wider range of injury.

Progression of CKD: IRB application has been approved at PUHSC. U-M IRB is under review. Sample collection at PUHSC has started. Yaqin Wang, a PhD student from the lab of PUHSC PI Dr. Yuqing Chen, will be visiting U-M after his visa is approved.

Institutional Review Board Core

Drs. Yali Cong and Haihong Zhang are close to having MOUs for IRB-of-Record agreements with six of the seven hospitals.

Collaboration Core

Drs. Kolars and Huang visited China in June and July. During their visit, they participated in a symposium hosted by Chang Gung Hospital in Taiwan and signed an MOU with the hospital. After that, they coordinated and facilitated the 2016 grant review process with PUHSC. Eight new awards were made and are featured on the previous pages.

GI/Liver Program

IBS: At PUHSC, 53 IBS and 28 healthy controls completed the study. At U-M, 15 IBS and 7 healthy controls completed the evaluation. Preliminary studies showed that IBS patients had increased inflammatory tone and an increase in intestinal membrane permeability accompanied by visceral hypersensitivity. The team is currently examining whether these functional abnormalities are correlated to gut dysbiosis.
**project updates**

**Esophageal Cancer:** The team is analyzing the deep-sequencing data and performing computational modeling of the tumors’ clonal composition. Two of the tumors were later reclassified and are being analyzed separately for manuscripts.

**NAFLD:** IRB approval was obtained from both sites in late April. Patient enrollment began in May. As of July 25, UMHS enrolled 9/80 NAFLD patients and PUHSC enrolled 21/160 NAFLD patients.

**Pulmonary Program**

**Pollution and Asthma:** In all, 25 out of a targeted enrollment of 50 patients in Beijing with moderate-to-severe asthma have been recruited. DNA from both whole blood and isolated T cells has been collected from these patients at different time points for eventual DNA methylation analysis of targeted genes. Studies of bronchial epithelial cells have shown that genes critical to asthma (TNFalpha, IL-13, ADAM33) are differentially expressed when exposed to particulate matter from Beijing, and DNA methylation changes in these genes are actively being investigated.

**COPD:** IRB has been approved at both PUHSC and UMMS. BAL, sputum and serum samples collected as a component of the multicenter SPIROMICS network have been formally requested and pulled, and shipping is anticipated within the next month. Patient recruitment is ongoing at PUHSC. Wenqi Diao, PhD, will spend at least six months at UMMS working with Dr. Stringer on the metabolomics analysis.

**Biorepository & Biomedical Informatics Core**

The BRBI Core continues to provide regular IT support for several JI projects on the acquisition, storage, and management of clinical information and bio-specimens. In addition to routine tasks, the team worked with IT support teams at both PUHSC and U-M to fix some unexpected internet connection interruptions.

**Other Projects**

**Epigenetic Effects of Prenatal Environment Exposures:** Student Zhen Shi has made great progress in DNA extraction and has visited U-M to learn more. The samples are expected to be ready for epigenetics chips in the next three months.

**PAD Severe Inflammation:** The IRB is under review. The team has carried out some animal studies similar to the JI project under the support of an MCubed grant. One manuscript has been submitted to *Scientific Reports*, and one abstract was sent to the 12th Annual Academic Surgical Congress on Aug. 22.
The JI collaboration model is touted as a successful institutional partnership in a paper recently published in *Academic Medicine*.

Written by leaders of the JI, the article highlights best practices, lessons and significant outcomes to emerge from the University of Michigan Health Systems’ partnership with Peking University Health Science Center. Detailed are the leadership and governance models for the JI.

“Institution-level collaborative partnerships across cultures are not without their challenges … including differences in governance structures, funding mechanisms … and intellectual property laws,” write the paper’s authors, led by Dr. Joseph Kolars. “One of the foundational aspects of the JI is that all decisions are made jointly … with a clear understanding that all decisions, including the dispersion of funds, will be agreed upon by both institutions.”

Between 2010 and 2015, the JI has funded 25 joint research projects involving more than 100,000 patients in both the US and China. The partnership appears on track for long-term sustainability.

“We are optimistic about the future of the JI because this model has been deemed valuable by the presidents of both institutions and has gained wide support among faculty,” the paper notes.