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JI Programs & Cores

Biorepository and Biomedical Informatics Core
Collaboration Core
IRB and Human Protection Core
Cardiovascular Disease Program
GI/Liver Disease Program
Pulmonary Disease Program
Renal Disease Program

Key to Commonly-Used JI Abbreviations

BRBI Biorespository and Biomedical Informatics
COPD Chronic Obstructive Pulmonary Disease
CVD Cardiovascular Disease
HCV Hepatitis C Virus
HDL High-density Lipoprotein
IRB Institutional Review Board
MI Myocardial Infarction
MICHR Michigan Inst for Clinical & Health Research
NIH National Institutes of Health
NSFC Natural Science Foundation of China
PUHSC Peking University Health Science Center
UM University of Michigan
UMHS University of Michigan Health System
UMMS University of Michigan Medical School
Dear Colleagues:

We are so pleased to tell you that planning is complete for the annual symposium, which will be held in Beijing October 26-28, 2015. Attendance is expected to exceed the first four meetings and will include several new faces. A snapshot of the symposium can be found on page 8 of this newsletter.

In this issue, we announce the newly funded JI investigative teams and projects. We also share with you some of the research and educational exchanges between PUHSC and UMMS that have taken place over the past few months. In addition, we highlight the activities of the Acute Aortic Dissection (AAD) project and provide updates on other research programs. Finally, we are pleased to share information about President Schlissel’s recent visit to PUHSC.

As always, we look forward to working together as we strive for major discoveries that will improve the health and quality of life for people around the world. Please feel free to submit news and suggestions for future issues to Dr. Amy Huang (yanhuang@umich.edu), Director for China Programs at UMMS, or Professor Qiudan Sun (sunqd@bjmu.edu.cn), Director, Office of International Cooperation at PUHSC.

Weigang Fang, PhD                      Joseph C. Kolars, MD
Co-Director, UMHS-PUHSC JI                   Co-Director, UMHS-PUHSC JI
Vice President                              Senior Associate Dean
Peking University                          Education and Global Initiatives
Health Science Center                      Josiah Macy, Jr., Prof. of Health Professions Education
Professor of Pathology                     University of Michigan Medical School

Student & Trainee Opportunities
The JI has exciting exchange opportunities available for students, trainees, fellows, and residents from UM and PUHSC. These opportunities are limited in number and are thus highly competitive. If you are interested in more information, please contact Amy Huang (yanhuang@umich.edu) and Qiudan Sun (sunqd@bjmu.edu.cn).
Education, Training, and

President Schlissel explores UMHS-PUHSC Joint Institute during China trip

UM President Mark S. Schlissel traveled to China July 5-11 to continue to build relationships with leaders of Chinese partner institutions and strengthen relations with international alumni. The president's trip began in Beijing where he experienced, firsthand, the partnership between the UMHS and PUHSC Joint Institute for Translational and Clinical Research (JI), which was founded in 2010. The JI seeks to catalyze pilot projects on diseases of interest to both countries. Twenty-five of the 29 departments at the UMMS have been involved with the JI. President Schlissel received an overview of the JI's cardiovascular, liver/GI, pulmonary, and renal research programs, and toured clinical facilities and research laboratories at the PUHSC Third Hospital.

In addition to President Schlissel, other UM-affiliated visitors to PUHSC in July included Barbara Ackley, Assistant Vice President for Development; James P. Holloway, Vice Provost for Global and Engaged Education; S. Jack Hu, UM’s Interim Vice President for Research; Amy Huang, Director for China Programs for Global REACH; Joseph C. Kolars, Senior Associate Dean for Education and Global Initiatives, UMMS; Richard Rogel, UM graduate, benefactor, and special advisor to UM and the JI; Debing Su, Mandarin content producer for Michigan News; and Zhong Wang, Associate Professor of Cardiac Surgery.

During their visit, the University of Michigan delegation also visited the Ministry of Education of the People's Republic of China and met with Vice-minister Huiqing Lin. Dr. Lin introduced the challenges and strategies of higher education in China. She also mentioned that a Sino-US cooperation like the UMHS-PUHSC Joint Institute was a successful example of a mutually-beneficial relationship. President Schlissel said that he selected China for his first overseas trip because UM has deep historical ties with the country and successful research collaborations with the nation’s top university. He expressed hope that the exchanges and cooperation in education and research would be strengthened in the future.
Delegation Visits

In February 2015, a delegation from Peking University (Mr. Yu Wang, Professors Shandong Xu, Yan Xu, and Lei Guo) visited UM. Their visit included meetings with several schools and departments (alumni association, intellectual property department, Ross School of Business and School of Engineering). They also met with faculty in Michigan Institute for Clinical & Health Research (MICHR), Learning Health Sciences, and Medical Student Education. In addition, they toured the University Hospital, CS Mott Children's Hospital, Biomedical Science Research Building, and Simulation Center.

In April 2015, Professor Qiudan Sun, Director of International Cooperation Office, and Dr. Weiming Wang, Director of Medical Education from PUHSC, met with faculty in MICHR, Learning Health Sciences, and Medical Student Education. They discussed topics on medical education reform, curriculum integration and implementation, and student assessment and evaluation. They also toured University Hospital and the Clinical Simulation Center.

Four PUHSC students, Mingzi Yang, Huilun Wang, Zhengxiang Huang, and Beini Liu, began their month-long laboratory training in July 2015. The purpose of the training is to expose the students to the research topics and environments at UM. The experience will allow students to “try out” laboratories and help students decide if they would like to apply to the PhD program at UM. Similarly, this will allow mentors to evaluate prospective students.
Acute Aortic Dissection (AAD) is the most common thoracic aortic emergency and may be rapidly fatal without early diagnosis and appropriate management. It is highly lethal, and an untreated type A dissection has a mortality rate of 1-2% per hour after the onset of symptoms. Surgical repair can transform the high mortality risk to an 80-90% chance of survival, and shortening the time from onset of symptoms to surgical treatment may greater reduce mortality rates. However, evidence suggests that in the United States, 50% of patients have a time to diagnosis of more than 15 hours after the patients arrive at the hospital. Thus, there is a critical need for AAD rapid diagnostic tools.

In 2013, the Joint Institute funded a research project “Identify Smooth Muscle Cell Specific Protein as Biomarkers for Early Diagnosis of Acute Aortic Dissections,” which aims to identify proteins in the serum of AAD patients as candidate biomarkers for AAD (since no ideal biomarkers currently exist), thereby providing the critical early diagnosis to improve patients’ chances of survival.

According to Dr. Bo Yang, Assistant Professor of Cardiac Surgery, UMMS, and co-investigator on the project, “The incidence of AAD is relatively low compared to acute coronary syndrome. In the US, if a center performs more than 13 AAD surgeries per year, it is considered to be an AAD high volume center.” He adds, “the advantage of the JI collaboration is that both the University of Michigan Health System (UMHS) and Peking University Health Science Center (PUHSC) have access to large populations of AAD patients and research infrastructure to perform all proposed experiments.”

The UMHS Cardiovascular Center treats approximately 50 AAD patients each year, while PUHSC Third and other affiliated hospitals conduct 100-200 AAD surgeries annually. Both institutions also have the proteomics core facilities and laboratory support necessary to measure smooth muscle cell (SMC)-specific proteins in the serum.

Dr. Yang is very satisfied with the progress at UMMS and with the research partnership. “We are very glad to collaborate with Dr. Zhe Zhang’s team,” shares Dr. Yang. “Dr. Zhe is a great partner and we communicate on a weekly basis.” “The data analysis of proteomics at UM has been completed,” he continues, “and the research team identified 5 target proteins as potential biomarkers of AAD. The PUHSC team will now conduct the proteomics study and confirm the target proteins.”

Dr. Bo Yang presented the AAD project update at 4th JI symposium
Acute Aortic Dissection Project

Investigators from both institutions formed a collaborative relationship in 2011 when Dr. Zhe Zhang visited UMHS to observe adult cardiac surgery cases and cardiac transplantation surgery. Dr. Zhe Zhang is Associate Professor of Cardiac Surgery Department, PUHSC Third Hospital, and serves as the PUHSC co-investigator for the project.

“The JI project offers a great opportunity for both institutions to access a larger patient population,” Dr. Zhe points out. “In addition, the collaboration allows our teams to learn how to do research following standardized procedures, including IRB submission and protocol development. Following a standardized process ensures a reliable and accurate result,” he explains. “If it is possible, I would like to send my graduate students to UMMS and learn how research is conducted in the United States.”

There were some challenges in the early stages of the project; for example, the time between the onset of symptoms and blood sample collection was much longer than expected at PUHSC. But through efficient communication between the two teams, the Co-PIs modified the methodology by collecting the samples at several time points and creating the curve to observe the change of related protein levels, which solved the problem.

Dr. Zhang also mentions his appreciation to the JI platform. In addition to the research collaboration, Dr. Zhang also appreciates the opportunity the JI provides to observe cardiac surgeries in the US. In August 2015, he visited Ann Arbor and met Dr. Frank Pagani, Professor of Cardiac Surgery, and discussed possible implantation of the first Heart Disease and the Left Ventricular Assist Device (LVAD) in China. If this is achieved, it would be extremely exciting news for the Chinese cardiac surgery society and would, ultimately, contribute to patients who are waiting for heart transplant.

Should the JI project be successful, the partners will generate crucial preliminary data to support grant applications for further clinical study with a larger number size through the NIH (USA) and the National Science Foundation (China).
At A Glance

Cardiovascular Program

**Dysfunctional HDL:** UM has completed sample analysis on all PUHSC samples. Five peer-reviewed publications have already resulted from this funding and one research paper is currently being written based on this work. **Atrial Fibrillation:** UM investigators have completed the initial study aimed at determining the mechanism of the transition from paroxysmal to persistent atrial fibrillation. The first pacemaker implantations at PUHSC were successfully performed. **Myocardial Infarction:** Genotyping of ~200,000 coding variants in 7,768 samples including 1,764 MI cases have been completed. A paper on initial findings is currently under review. **Cell Therapy Against Cardiovascular Disease:** IRB for collecting patient cells has been submitted at both UM and PUHSC and the UM protocol has been approved. The chemical approach for generating induced pluripotent stem cells (ciPSCs) from mouse cells has been successfully completed at UM with guidance from the Deng Laboratory at PUHSC. The proposed experiments to generate human ciPSCs are being carried out. **Brain Iron Overload:** In April 2015, the project was awarded a R01 grant of $1.09 million from NIH. **Acute Aortic Dissection:** Featured on pages 4 and 5.

Renal Program

**CKD Prognosis:** Candidate CKD molecular markers were identified by both sites and are being cross-validated. The first manuscript received a favorable review in *Science Translational Medicine* and is currently under revision. One abstract has been accepted as a talk to be presented at the American Society of Nephrology’s Annual Meeting, 11/5/2015. Data from the project is serving as preliminary data for the grant proposal submitted to the Juvenile Diabetes Research Foundation’s consortium. **CKD Comparison:** A research poster on comparison of the prevalence and differential impact of risk factors for CKD in China and the US was presented at the World Congress of Nephrology Conference in March 2015. The team is currently developing a manuscript for submission to a peer reviewed journal.

Institutional Review Board Core

On June 15, 2015, Peking University received full accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP). AAHRPP promotes high-quality research through an accreditation process that helps organizations worldwide strengthen their human research protection programs (HRPPs). AAHRPP uses a voluntary, peer-driven, educational model to ensure that HRPPs meet rigorous standards for quality and protection. To earn accreditation, organizations must provide tangible evidence through policies, procedures, and practices of their commitment to scientifically and ethically sound research and to continuous improvement. AAHRPP accreditation offers assurances to research participants, researchers, sponsors, government regulators, and the general public that an HRPP is focused first and foremost on excellence.
GI/Liver Program

HCV: Enrollment goal of 2,000 patients was reached in July. Two abstracts were accepted for poster presentation at the 2015 AASLD Liver Meeting, and a proposal on analytic morphomics and NAFLD (fatty liver) was submitted in response to the 2015 JI RFP. In summer 2015, three M1 students, Jeremy Balch, Mary Guan, and Jiaxin Huang, completed a survey study on HBV knowledge and stigmatization in Beijing as part of their global health experience. Dr. Ming Yang, hepatologist at PKU completed her 1-year Fogarty Fellowship in July 2015. IBS: IRB has been approved at both PUHSC and UMMS. Both sites are actively recruiting subjects with IBS and healthy controls.

Pulmonary Program

Pollution and Asthma: IRB has been approved at both PUHSC and UMMS and the project is ready to implement.

Biorepository and Biomedical Informatics Core

Besides providing regular IT support for several JI projects on the acquisition, storage, and management of clinical information and bio-specimen, the BRBI Core works with PUHSC CRI researchers on the adoption of Open Clinical for their other research projects and the building of a more efficient, secure and scalable IT infrastructure for their clinical research activities. Professors. Huiyin Qi and Shibin Song from PUHSC IT departments visited UM at the end of April. The main purpose was to meet BRBI core researchers at UM and communicate on different clinical and sample information management platforms, IT infrastructure setup for data management and high performance computing and biomedical data analysis issues. During their visit, they met Dr. Ted Hanss, CIO of UMMS and discussed IT management and support issues. They also visited the Pathology Department biorepository to learn the operation procedure, software, and hardware setup.

Collaboration Core

Collaboration Core coordinated and facilitated the 2015 grant review process. Seven new awards were made and are featured on page 9.

Other Collaborative Projects

Radiology: IRB has been approved at both PUHSC and UMMS. The study team has started working with clinical collaborators for patient recruitment. Esophageal Cancer: IRB has been approved at both UM and PUHSC. SNP genotyping and exome sequencing data for over 130 samples from 13 tumors have been collected and are being analyzed. Preliminary results were presented at the American Association of Cancer Research meeting in April and the Cold Spring Harbor Laboratory genome meeting in May. Epigenetic Effects of Prenatal Environment Exposures: The project has received IRB approval and reconsenting will start soon.
5th Joint Institute Symposium, October 26-28, 2015
BEIJING, CHINA

October 26, 2015
JI Program Concurrent Sessions
Break-out Group Meetings
Team Dinner

October 27, 2015
Opening Ceremony
Keynote Speeches
Thematic Cross-Disciplinary Sessions
Poster Session
Joint Institution Banquet

October 28, 2015
Thematic Cross-Disciplinary Session
JI Project Progress Reports
Wrap-up Meeting
Closing Remarks

Keynote Speakers

In pursuit of disease drivers across continents and disciplines: tales from a renal road warrior
Matthias Kretzler, MD
Professor of Internal Medicine, UMMS

Hematologic malignancy development from China perspective: past to present
Xiagojun Huang, MD
Chairman and Professor of Institute of Hematology, PUHSC

Thematic Cross-Disciplinary Sessions
I. Science of Collaboration
Anna Lok, MD, Research Professor of Hepatology and Professor of Internal Medicine, UMMS
Hong Zhang, MD, PhD, Professor of Renal Department, First Hospital, PUHSC
Yangfeng Wu, MD, PhD, Executive Associate Director, Clinical Research Institute, PUHSC

II. Big-Data
Brian Athey, PhD, Professor & Chair of Computational Medicine and Bioinformatics
Professor of Psychiatry and Internal Medicine, UMMS
Co-Director, Michigan Institute for Data Science
Kevin Ward, MD, Professor of Emergency Medicine
Executive Director, Michigan Center for Integrative Research in Critical Care
Executive Director, Fast Forward Medical Innovation, UMMS
Andrew Rosenberg, MD, Associate Professor of Anesthesiology and Internal Medicine
Chief Medical Information Officer, UMMS
Yonghua Hu, MD, Executive Deputy Director, PUHSC
Tim Hubbard, PhD, Head of Medical and Molecular Genetics Department, King’s College London

III. Pollution
Robert Brook, MD, Professor of Internal Medicine, UMMS
Min Hu, PhD, Director, State Key Joint Laboratory of Environmental Simulation and Pollution Control, Peking University
Wei Huang, ScD, Professor of Occupational and Environmental Health Sciences, PUHSC
Frank Kelly, BSc, PhD, Director of Environmental Research Group and Deputy Director of the MRC-PHC Centre for Environment and Health, King’s College London
Introduction to New 2015 JI Projects

**Urine Protein Glycosylation and Progression of Chronic Kidney Disease**
Subramaniam Pennathur, MD, Associate Professor of Internal Medicine, UMMS
YuQing Chen, MD, Professor of Nephrology, First Hospital, PUHSC

**Prevention of Kidney Failure in Alport Syndrome by Application of Podometric Technology**
Roger Wiggins, MB, BChir, Professor Emeritus, Internal Medicine, UMMS
Jie Ding, MD, Professor of Pediatrics, Vice President, First Hospital, PUHSC

**Compartmental Analysis of Metabolite Profiles Associated with Disease Phenotypes in Chinese and US Smokers With and Without COPD**
Theodore Standiford, MD, Professor, Internal Medicine, UMMS
Bei He, MD, Professor and Director of Pulmonary Medicine, Third Hospital, PUHSC

**Lipidomic Markers for Coronary Artery Disease**
Eugene Chen, MD, PhD, Frederick G. L. Huetwell Professor of Internal Medicine, UMMS
Guisong Wang, MD, Professor of Cardiology, Third Hospital, PUHSC

**Risk-Adjusted Outcome Prediction for Emergency Department Intensive Care Unit Patients**
Kyle Gunnerson, MD, Associate Professor of Emergency Medicine, UMMS
Qingbian Ma, MD, Vice Director and Associate Professor of Emergency Medicine, Third Hospital, PUHSC

**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 PUHSC**
Anna Lok, MD, Professor of Internal Medicine, UMMS
Lai Wei, MD, Director and Professor of Hepatology Institute, Vice President, Second Hospital, PUHSC

**Targeting Peptidylarginine Deiminase for Diagnosis and Treatment of Trauma and Sepsis**
Hasan Alam, MD, Professor of Surgery, UMMS
Baoguo Jiang, MD, Vice President of PUHSC, Professor of Orthopedics and Traumatology, Second Hospital
Executive Officers of the University of Michigan Health System: Marschall S. Runge, MD, PhD, Executive Vice President for Medical Affairs; James O. Woolliscroft, MD, Dean, U-M Medical School; T. Anthony Denton, JD, MHA, Acting Chief Executive Officer; Kathleen Potempa, PhD, Dean, School of Nursing.

The Regents of the University of Michigan: Michael J. Behm, Mark J. Bernstein, Laurence B. Deitch, Shauna Ryder Diggs, Denise Ilitch, Andrea Fischer Newman, Andrew C. Richner, Katherine E. White, Mark S. Schlissel, (ex officio).

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