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JI Programs & Cores

Key to Commonly-Used JI Abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>BRBI</td>
<td>Biorepository and Biomedical Informatics</td>
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<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<td>CRI</td>
<td>Chinese Research Institute</td>
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<td>CVD</td>
<td>Cardiovascular Disease</td>
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<td>HCV</td>
<td>Hepatitis C Virus</td>
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<td>HDL</td>
<td>High-density Lipoprotein</td>
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<td>IRB</td>
<td>Institutional Review Board</td>
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<td>MI</td>
<td>Myocardial Infarction</td>
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<td>MICHR</td>
<td>Michigan Institute for Clinical &amp; Health Research</td>
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<td>NIH</td>
<td>National Institutes of Health</td>
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<td>NSFC</td>
<td>Natural Science Foundation of China</td>
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<td>PUHSC</td>
<td>Peking University Health Science Center</td>
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<td>U-M</td>
<td>University of Michigan</td>
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<td>UMHS</td>
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<td>UMMS</td>
<td>University of Michigan Medical School</td>
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April 2014

Dear Colleagues:

The first Joint Institute (JI) newsletter of 2014 finds us all enjoying Spring’s welcome. After setting a record for the snowiest winter ever on March 12th, milder temperatures are most welcome to those of us in Ann Arbor.

In this issue, we are pleased to share with you recent honors of two of our JI faculty from Peking University Health Science Center (PUHSC) and some of the research and educational exchanges between PUHSC and the University of Michigan Medical School (UMMS) that have taken place over the past few months. We highlight the activities of the Institutional Review Board and Human Protections Core and provide updates on the other Cores and the research programs. We also include an update on the 2014 JI Call for Proposals.

Finally, we remind you of the upcoming Fourth Annual Joint Institute Symposium, which will take place in Ann Arbor October 1-3, 2014. Details are still emerging, but please put this on your calendars now.

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 (UMMS) or Professor Qiudan Sun (sunqd@bjmu.edu.cn), Director, Office of International Cooperation at PUHSC.

Student & Trainee Opportunities

The JI has exciting exchange opportunities available for students, trainees, fellows, and residents from U-M 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).

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The Joint Institute Celebrates

Professor Yang Ke, Executive Vice-president of Peking University and Peking University Health Science Center (PUHSC), was one of seven health professional educators recognized at the January 2014 Prince Mahidol Award Conference in Pattaya, Thailand. The Excellence in Health Professional Education awards are given to those honorees whose work has had a strong impact on the improvement of health care through their dedication to teaching, learning, and education.

In recognizing Professor Ke, the conference website noted the following: “Professor Ke is in charge of all issues related to education of health professionals. In the past 10 years, she and her team have played an important role in studying China’s education of health professionals and providing the government with research evidence and suggestions for medical technology development, healthcare reform, and education reform. Professor Ke is a passionate leader in reforming teaching modules at PUHSC, which aim to strengthen medical students’ professionalism and overall competencies, reform curricular systems under the principles of autonomous learning and problem-based learning, and provide medical students with more exposures to primary care practice. Under her leadership, a number of new majors/disciplines were established or strengthened at PUHSC.”

Following successful meetings at the 2013 Joint Institute Symposium in Beijing, the University of Michigan Kidney Epidemiology and Cost Center (UM-KECC) is delighted to announce that Professor Fang Wang has been selected to be an International Society of Nephrology (ISN) visiting scholar at KECC beginning June 2014. Each year, the ISN Fellowship Programs awards approximately 30 fellowships to nephrologists from developing nations for hands-on training at host institutions that can offer state-of-the-art knowledge in basic and clinical nephrology, dialysis, epidemiology, and transplantation. Professor Fang Wang will be dual-mentored in the epidemiology of renal disease by Professor Haiyan Wang (PUHSC) and Dr. Rajiv Saran (UM-KECC).

KECC is an interdisciplinary research group dedicated to fighting the battle against kidney disease. Founded more than twenty years ago, KECC includes nearly thirty academic leaders from medicine, public health, pharmacy, and economics.

Four Peking University Health Science Center students participated in a month-long clinical elective at the University of Michigan Medical School during November and December 2013. Shown (left to right) are Jing Song (Internal Medicine), Zexuan Wu (Psychiatry and Radiology), Yuebo Jin (Surgery and Emergency Medicine), and Meng Yu (Neurology).
New Awards and Scholarly Exchanges

Four Residents of the University of Michigan Medical School each spent a few weeks in training at PUHSC during Winter 2014. The residents included Drs. Ashmita Chatterjee (Pulmonary Medicine, mentored by Drs. Ning Shen and Bei He, Third Hospital); Amanda Guentner (GI/Hepatology, mentored by Drs. Anna Yuan, Huiying Rao, and Lai Wei, Second Hospital); Emily Perdoncin (Cardiology, mentored by Drs. Yan Zhang and Yong Huo, First Hospital); and Rina Verma (Cardiology, mentored by Drs. Wang Guisong and Wei Gao, Third Hospital).

According to Dr. Guentner, she was looking to learn more about how healthcare is delivered in Asia, specifically gastroenterology and cardiology. “I was curious to observe how well patients tolerate procedures with minimal sedation, as I wonder if we sometimes over-use sedating medications in the US.” She adds that she was able to integrate into an incredibly foreign and new environment as well as could be expected, working collaboratively with, and learning from, the Chinese healthcare workers. “I especially enjoyed interacting with the interns during education sessions and trying to bypass the language barrier to talk about our common interest of GI.”

Dr. Verma notes that she accomplished her main goals for this experience: to learn about different diseases processes and to learn how culture and different belief systems can impact medical practice. She was particularly impressed with the importance of family in medical treatment and clinical decision-making. “Family is much more involved in medical care in China than in the US,” she reports. Even to the point where “family members must sign their loved one’s consent form prior to procedures and are involved in transporting patients.”

Professor Yang Yang, MD, an attending physician from PUHSC First Hospital, is near the end of his one-year Joint Institute fellowship. Since last June, he has used the time off from his clinical responsibilities to collaborate with cardiovascular research investigators in Dr. Santhi Ganesh’s laboratory and gain valuable cardiology research experience.

Professor Yang notes that one year is not enough time to become an expert in anything, but the experience “has allowed me to learn basic research elements, apply my statistical skills in analyzing data, and understand the work flow within a research setting.” He adds that it is his hope to “be able to transfer some of my new research knowledge into my clinical practice, and perhaps have an opportunity to stay involved in this research at PUHSC.”

He expressed his appreciation for all of his experiences, but especially the ability to attend grand rounds and research-specific seminars. “I particularly liked the process of the grand rounds presentations,” he shares. “Rather than just lay out an entire case study or clinical information, the presenters would limit the amount of information given at a time and ask what we would do. This gave us an opportunity to think more deeply about treatment and align our answers with how we would respond and behave in actual clinical practice.”
Institutions that perform research using human subjects are required to meet specific standards and obtain formal approval from a governing body known as an Institutional Review Board (IRB). From informed consent of participants to delineated responsibilities of all investigators, from protected health information to payment of research subjects, from blood draw and tissue sampling guidelines to accessing medical records; investigators submit, and IRBs carefully examine, a large laundry list of required elements for each proposal. For collaborative research projects performed across international boundaries, such as those within the Joint Institute for Translational and Clinical Research (JI), this means securing approval from the IRBs of both institutions involved as well as meeting country-specific standards when governmental funds are used.

According to Dr. Michael Geisser, Professor of Physical Medicine & Rehabilitation at the University of Michigan and a member of the JI IRB and Human Protection Core, “from a human subjects protection standpoint, meeting the ethical standards that satisfy both institutions with regard to collaborative projects has certainly involved more work and oversight than were we treating the investigator at each institution as separate investigators. Cultural differences make their way into the research world and have an influence on the IRB standards and protocols that have been established.” “Although most countries follow basic ethical principals,” he explains, “clearly-defined international ethical codes for human subjects don't exist. This has challenged us to be thoughtful and strategic in guiding JI investigators to submit research proposals that meet the IRB guidelines of both institutions.”

Two specific areas where JI proposals have required the most consideration are informed consent and criteria for genetics research. Generally speaking, US institutions consider rights of privacy to be of utmost importance in participation of human subjects, granting autonomy to the individual and disallowing the use of any personal identification. China, on the other hand, has typically viewed right to consent in the historic lens of a paternalistic society. There are also ethical challenges for banking, sharing, and using genetic data and samples. “China has long felt that international researchers have come in and taken advantage of their genetic resources,” points out Geisser. “So, in the 1990s, he adds, “they developed stringent criteria for genetics research and now have a separate governing panel that reviews whether or not it is okay to share genetic data/samples with researchers outside of China.” As all of the JI projects involve some type of genetic sampling, the new criteria apply. Though most JI data are now stored on a central server at U-M, a genetics firm in China handles all of the analyses and all samples are approved before transfer.

Advanced technology has further enlivened the conversation by pushing both informed consent and genetics research into an arena that few could have predicted. IRBs are now faced with consent considerations for future research. “Technology is advancing at such a fast rate that it is brings its own challenges,” Geisser explains. “A research consent form 15 years ago couldn’t foresee how valuable some samples might be, and all of the possible uses of these materials. So do you re-consent past subjects? Do you alter current language so that participants consent to future research with few details as to what this might be? How do we articulate or even envision what future research on stored samples may look like?”
to the Joint Institute Mission

Ethical challenges from biospecimens and health information: A perspective from PUHSC

With the development of the JI, the PUHSC and the U-M IRB Core team has worked hard to facilitate the research ethics challenges of the JI investigators. Due to the different research styles and resources, the IRB Core partnership has gradually discovered and confronted differences that exist between institution-wide and country-wide IRB requirements. Privacy information, for instance, is regulated by HIPPA in the United States, yet lacks similar regulation in China; and while China has recently established some mutual biobanks, implementing the secondary use of the biospecimens is still an evolving process. Sending sample information from China to the United States requires careful collaboration, and human genetic data is a particularly sensitive topic given that China has very specific national regulations that collaborating international institutions must adhere to.

Professor Yali Cong, Chair of the Institutional Review Board and faculty in the Department of Medical Ethics at PUHSC, also echoes Dr. Geisser's concern about the challenges in obtaining re-consent from past subjects. Identifiable blood samples that were once obtained for research purposes hold informed consent for original studies, but the original consent forms made no mention of continuous or future use. Once an original study has been completed, it may be difficult to contact patients to obtain re-consent due to insufficient contact information on the Informed Consent Form (ICF). Some researchers don't keep samples after the projects are complete and the challenge ends there. Most researchers, however, reject the thought of discarding samples that may still provide value and then have to wrestle with the nuances of previously unanticipated ethical practices.

According to Professor Cong, the JI IRB Core has been, and will continue to be, essential in helping researchers deal with issues by reviewing risks to subjects, practicability for re-consent, research values, and balancing all of the factors involved. In union with Dr. Geisser's perspective, she poses similar considerations for JI projects:

- When informed consent for tissue/blood collection was for a clinical diagnosis purpose, and the clinical work is complete, what happens when future researchers want to do research using these identifiable biospecimens? Is there an honest broker to separate the individual information from researcher? How can privacy information be protected?
- When original ICF forms note that samples will be used in a general disease area, but the description is not specific enough for current regulations; or whether the proposed secondary research can reasonably be understood to fall within the scope of research that was described in the original consent form; what are the available options?
- The set up of the bio-repository now requires a separate application for IRB approval. But oftentimes this procedure didn't previously exist. What does one do in this situation?
- When new research use imposes new or significantly greater risks not described in the initial consent form, what are our responsibilities?
At A Glance

Cardiovascular Program
Dysfunctional HDL: Recruitment of subjects is near completion at both sites with 140/160 planned subjects enrolled. PUHSC has completed transfer of 50 samples to U-M; final shipment will occur once enrollment is completed. Extensive joint training has been conducted with 5 trainees from PUHSC. Three peer-reviewed publications have been published thus far and one more research paper is in review. Plans for potential grant submission from results stemming from this work to Chinese granting agencies is under way. Atrial Fibrillation: The first in-vivo experiments are being set up. PUHSC collaborator, Dr. Lin Wu, visited in April to observe surgical procedures for implantation of transvenous pacemaker catheters using an animal model and to help determine project protocols. Two U-M research associates will travel to Beijing to help PUHSC investigators on a related project. Air Pollution and HDL: IRB approval at U-M has been received and is pending at PUHSC. A great deal of communication has taken place to harmonize study protocols. The U-M portion of the study, including patient enrollment, is on schedule for mid-end May. The team is setting up the database model and developing the corresponding statistical methodology. Acute Aortic Dissection: IRB approval has been received and initial blood samples from patients has been collected. Communication between partner investigators is happening on a weekly basis. Brain Iron Overload: The proposed studies have been carried out. Five ICH patients have been enrolled in Beijing and three ICH pigs have been done (have MRI )at U-M. Myocardial Infarction: To attempt to identify novel variants and genes associated with myocardial infarction and blood lipid levels in Chinese samples, genotyping of ~200,000 coding variants in 7,768 samples, including 1,764 MI cases, have been completed. Samples were collected from PUHSC First and Third Hospitals as well as community hospitals in Beijing and Wuhan. Blood Pressure Genetics: The team completed preliminary statistical association testing and generated initial findings. A paper has been submitted based on the initial results. Visiting scholar Yang Yang from PUSHC First Hospital will finish his one year training at Dr. Ganesh's lab and return to PUHSC in May.

Pulmonary Program
COPD: The JI Pulmonary group at U-M was awarded a $600,000 supplement award from the NHLBI Global office through the Centers of Excellence program to combat non-infectious chronic diseases. U-M served as the data coordinating center, the sequencing and bioinformatics center, and the biostatistics center, as part of a four-site international study of the Pulmonary Microbiome in COPD. The countries involved in addition to U-M in the USA and PUHSC Third Hospital in China, were Peru, Nepal, and Bangladesh. Despite a very tight time line for this project (9 months) data was reported at the recent NHLBI Global Centers of Excellence meeting in Bethesda. NHLBI leaders enthusiastically responded to the work at the meeting. The JI pulmonary group has submitted a proposal investigating the Lung-Gut microbiome in collaboration with John Kao (U-M GI).

Other Collaborative Projects
Radiology: Dr. Dong submitted her application to the Cancer Center Protocol Review Committee in February and presented the protocol to the committee in late April. Once her protocol is approved, the team will file IRB applications at both UMMS and PUHSC.
Liver Program
HCV: Total enrollment includes almost 1600 patients. Preliminary data was presented in early April at the European Association for the Study of the Liver meeting in London. Drs. Lai Wei, Huiying Rao, and Anna Lok attended. Dr. Lok and Ms. Elizabeth Wu will visit Beijing in July when Ms. Fanny Du, an M1 student, and Ms. Angela Xie, a U-M undergraduate student, will be carrying out a summer project as part of their global health experience. Dr. Ming Yang, working with Professor Wei, was awarded an 11-month Fogarty Fellowship in Global Health to investigate patient knowledge regarding their liver disease and explore their satisfaction with patient care. She will be co-mentored by Drs. Wei and Lok.

Renal Program
Experiments emerging from the longstanding collaborations are accelerating quickly in the joint project. Dr. Wenjun Ju will visit PUHSC in June to coordinate current studies with Professors Haiyan Wang, Minghui Zhao, and Hong Zhang including data analysis, results discussion, and planning for manuscripts. Professor Fang Wang (PUHSC) has been awarded an International Society of Nephrology visiting scholarship at the U-M Kidney Epidemiology and Cost Center (UM-KECC) beginning June 2014. Professor Fang Wang will be dual-mentored in the epidemiology of renal disease by Professor Haiyan Wang (PUHSC) and Dr. Rajiv Saran (UM-KECC).

Biorepository and Biomedical Informatics Core
The BRBI Core continues to provide laboratories and IT applications support for the acquisition, storage, and management of bio-specimen and case report forms; solutions that integrate with PUHSC hospital information systems to acquire clinical and administrative data; and assistance in establishing high-throughput computing platforms for clinical phenotyping and analysis. In addition, this Core has created shared data ownership and data stewardship responsibilities; helped to coordinate export permit applications and shipping of bio-specimens out of China; and developed and implemented data auditing and triangulation plans to address potential quantitative analysis and trust issues.

Collaboration Core
With the Collaboration Core's coordination and facilitation, 17 joint proposals were submitted in response to the JI 2014 RFA and are currently under review at both MICHR and CRI. The new joint MD/PhD program will welcome its first cohort students this fall; two students from PUHSC will be enrolled in the UMMS Program in Biomedical Sciences to pursue their PhD degrees. New team member, Ms. Yi Mao, was introduced to the Collaboration core at UMMS. Ms. Mao will work with the JI management team and assist Dr. Amy Huang in the JI operation and management.

Institutional Review Board Core
The IRB Core is featured on pages 4 and 5; there are no other updates to include.
Update on the 2014 JI Call for Proposals

In each of the past two years, the Joint Institute (JI) put out calls for proposals for pilot funding of projects that would demonstrate an effective team approach to discovery and new findings on diseases relative to both China and the US, and which could be leveraged for extramural funding opportunities. Six awards were made in 2013.

The 2014 “Call” yielded seventeen proposals including applications from 30 investigators not previously funded by the JI. Proposed research topics included epigenetic changes in gastric cancer genes, effects of prenatal environmental exposures, monitoring of type II diabetes self-care activities, generation of patient-specific cardiac stem cells, use of bone filler materials to regenerate alveolar bone, and imaging of hepatocellular carcinoma.

Award announcements are expected to be made late spring/early summer. Anticipated start date for new projects is July 1, 2014.

Joint Institute Symposium, October 1-3, 2014
SAVE THE DATE!

The Fourth Annual Symposium of the Joint Institute for Translational and Clinical Research will be held October 1-3, 2014 in Ann Arbor, Michigan. Nearly 50 colleagues from Peking University Health Science Center are expected to participate in the multi-day event. The JI leadership retreat will be held prior to the symposium, a co-symposium with the Michigan Institute for Clinical and Health Research and the alumni dinner will be on October 1st, and the symposium banquet will be held on October 2. Days two and three will be dedicated to JI-specific work including concurrent sessions of the research programs and cores, keynote speeches and panel discussions, and reports from the JI programs. Stay tuned for further updates.
News From UMHS

March 2014
New collaborative agreements established this winter will foster educational and research initiatives between the University of Michigan Medical School and two institutions in China: Central South University Xiangya School of Medicine and Nanjing University School of Medicine. The collaborative education and research agreements will allow for exchange of faculty, researchers, and post-doctoral fellows. The agreements will also foster alliances in research and publication and enable education abroad opportunities both for U-M and Chinese medical and graduate students.

April 2014 – May 2014
Peking University Medical College students, Yuan Liu and Zhou Ying, participated in a four-week elective/medical clerkship in the U-M Emergency Medicine Department.

April 30, 2014 – May 2, 2014
A delegation from Harbin Medical University visited UMMS. Led by President Baofeng Yang, the group of four met with UMMS leadership and had a tour of Mott Children’s Hospital and CVC.

April 2014 - June 2014
Professor Qingbian Ma, Vice Director PUHSC Third Hospital Emergency Department, started a 3-month clinical observation in UMMS Emergency Medicine on April 1st.

News From PUHSC

January 2014
Professor Yang Ke, Executive Vice President of Peking University and Peking University Health Science Center (PUHSC), Professor Fang Weigang, Vice President of PUHSC, and other PUHSC colleagues extended a warm welcome to Dr. Marcia McNutt, editor-in-chief of Science, and Dr. Bill Moran, the global director of Custom Publishing, International Collaboration, and Advertising for Science Publications. Their one-day visit in January provided an opportunity to discuss peer-review procedures and to strengthen the relationship between Science and PUHSC.

March 2014
A progress seminar regarding the China Medical Board (CMB) MOOCs (Massive Online Open Courses) was held on March 20th at Peking University School of Distance Learning for Medical Education. Participants included leaders from CMB and faculty from MOOCs programs at PUHSC, Peking Union Medical College, Fudan University, and Sun Yat-sen University.

April 2014
Sixty-nine PUHSC students have been selected to participate in clinical rotations/electives during the upcoming academic year at prestigious medical institutions in Asia, Australia, Europe, and North America (including the University of Michigan).
Executive Officers of the University of Michigan Health System: Ora Hirsch Pescovitz, MD, Executive Vice President for Medical Affairs; James O. Woolliscroft, MD, Dean, U-M Medical School; Douglas Strong, Chief Executive Officer, U-M Hospitals and Health Centers; Kathleen Potempa, Dean, School of Nursing.

The Regents of the University of Michigan: Mark J. Bernstein, Julia Donovan Darlow, Laurence B. Deitch, Shauna Ryder Diggs, Denise Ilitch, Andrea Fischer Newman, Andrew C. Richner, Katherine E. White, Mary Sue Coleman (ex officio).

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