

PERSPECTIVE

Advancing science and education through a novel collaboration platform between the University of Michigan and Peking University Health Science Center

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Abstract

Research in China has been advancing over the past decade with increasing investments from government and private entities. Collaboration with Chinese investigators and those in the United States has also increased as reflected in the growth of scientific papers with Chinese authors. Collaborations are more commonly based on faculty-to-faculty relationships which can be challenged by institutional or governmental policies. This paper reports on an institution-to-institution collaboration, the Joint Institute for Translational and Clinical Research initiated in 2010 between the University of Michigan Medical School and Peking University Health Science Center, to enable and support collaborative faculty-initiated research. Concomitant education and training programs have also been co-developed. Beginning in 2011, 190 proposals from faculty-to-faculty partnerships have been submitted from which 59 have been selected for funding. These projects have involved over 138,000 patient subjects and resulted in 86 peer-reviewed publications to date. Pilot data has been leveraged to secure \$27.3 million dollars of extramural funding outside of China. Faculty and trainee exchanges take place regularly including an annual symposium with mechanisms to link faculty who are seeking partnerships by utilizing each other's complementary strengths and resources. As the collaboration enters its second decade, both institutions believe that the model offers a unique platform to promote faculty-initiated collaborative research. Next steps include funding studies in prioritized scientific themes, and promoting access to high-quality cohorts to attract industry partners and to develop sustainable financial models.

KEYWORDS

biomedical research, China, international educational exchange, support of research, translational medical research

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1 | INTRODUCTION

1.1 | Opportunities

The growth in science research and publications in China has been striking. The U.S. National Institutes of Health (NIH), the largest funder of biomedical and behavioral research in the world, has noted a 253% increase in papers with a Chinese co-author between 2009 and 2017 at a time when the overall NIH budget was flat.¹ By this parameter, China is the leading international collaborator on NIH-funded research. China has been increasing support for science and engineering research over the past decade and in 2017 accounted for 23% of the world's expenditure for research and development, closely rivaling the U.S. leadership at 25%.² One of the largest sources of support is the National Natural Science Foundation of China (NSFC) which allocated over 31 billion RMB (\$4.6 billion U.S.) in 2019.³ A growing number of entities have been established to advance the biomedical research in China including private companies such as the Beijing Genomics Institute.⁴ Collaborative research is being encouraged from governmental agencies in the United States and China such as joint programs between the U.S. National Science Foundation and China's NSFC.⁵ In the United States, the NIH has a U.S.–China Program for Biomedical Collaborative Research.⁶ Drivers for collaboration include access to students, trainees, research resources, and capacity building. Also, the research environment in China can be less costly than in the west.

1.2 | Challenges

Faculty may encounter challenges when trying to engage in collaborative research between the United States and China. First, transactional barriers such as differences in language,

time-zone, and communication styles (i.e., text vs. email vs. phone call) can be more easily overcome than the cultural differences in approaches to data integrity enforcement, authorship determination, and intellectual property allocation. Untested assumptions about how things work in one place are often erroneously generalized to the partner institution. Conflict resolution is typically culturally based and can easily become problematic if not resolved directly but diplomatically with a deep understanding of how disagreements and differences are managed in different settings. Second, collaborations between individual investigators can suffer from the absence of supportive, enabling institutional leadership while collaborations only between leadership can miss investigators' grassroots enthusiasm necessary to catalyze the innovative opportunities. Finally, governmental oversight in the United States and China can be influenced by political relationships between the countries that may present challenges for individual researchers to navigate.

With both opportunities and challenges in mind, the University of Michigan Medical School (UMMS) set out to establish a new institution-to-institution collaborative platform to facilitate faculty-initiated translational and clinical research in China. The purpose of this report is to extend the original report in 2017⁷ with a special emphasis on science research.

2 | APPROACH

2.1 | Overall framework and governance structure

As previously noted,⁷ the collaborative platform was established in 2010 as the Joint Institute for Translational and Clinical Research (JI) with the signing of a memorandum of understanding⁸ acknowledging plans to provide pilot funding

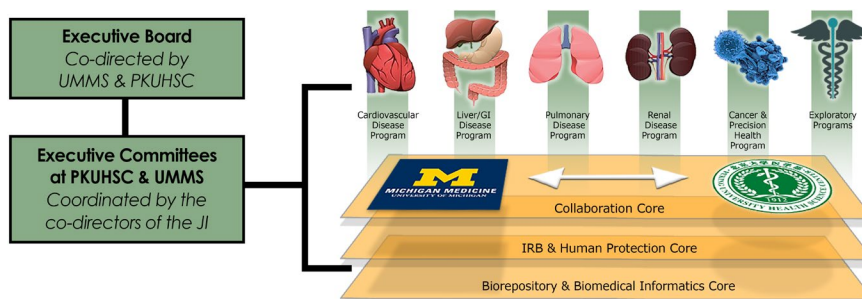


FIGURE 1 Governance structure, thematic research programs, and enabling cores of the Joint Institute (JI) for Translational and Clinical Research between Peking University Health Science Center (PKUHSC) and University of Michigan Medical School (UMMS). The Joint Institute (JI) for Translational and Clinical Research comprises six research programs: Cardiovascular Disease, Liver/GI Disease, Pulmonary Disease, Renal Disease, Cancer & Precision Health, and Exploratory. In addition, three enabling cores were established to facilitate the research, collaboration, and culture of inquiry. They are Collaboration Core, IRB & Human Protection Core, and Biorepository & Biomedical Informatics Core. The cores and research programs are overseen by the Executive Committee at each institution that are coordinated by the JI co-directors who report to the Executive Board

for co-investigator-initiated studies as well as research infrastructure (i.e., three enabling cores). The cores were established to facilitate the research, collaboration, and culture of inquiry that was desired. The cores and project proposal pathways are overseen by the Executive Committee at each institution that are under the stewardship of the JI co-directors (Joseph Kolars and Qimin Zhan) who report to the Executive Board Figure 1. An agreement outlining the governance of the JI decision-making process, authorship, and intellectual property was defined and agreed upon by the legal offices of both universities. Furthermore, the intended goals by which success would be measured at 5 years was clearly articulated and agreed upon by both sides. The overarching goal is the generation of collaborative studies that could be leveraged for external funding with results that would improve the understanding of diseases of mutual interest.

2.2 | Equal investment and equal partnership

Seven million dollars of funding was initially provided by each side to be spent on projects and enabling cores within their own respective institutions. Each of the enabling cores was jointly designed and managed by the faculty and staff at each institution. One of the foundational aspects of the JI is to ensure that all projects are investigator-initiated and that all decisions are jointly agreed upon. Each project requires co-Principal Investigators (PI) at each institution who collaboratively make decisions on developing the proposal, formulating the budget, and executing the project once funded. Funding for all projects receive equivalent monetary awards from PKUHSC and UMMS. The Executive Board and the Executive Committee consist of leadership from both institutions with a clear understanding that all decisions, including the dispersion of funds, will be jointly determined. Another defining element of the JI was ensuring that collaboration take place at the investigator level, most often working within the “thematic programs” that are co-led by investigators from both institutions Figure 1. These thematic areas were initially chosen based on the disciplinary interests of the leadership from both institutions who were originally interested in establishing a collaborative platform. These leaders also recognized that these themes include a substantial spectrum of burden of disease for both the United States and China such that novel or collaborative solutions may have significant impact for both countries. Initially, 20% of funding in each round of proposals was set aside for exploratory areas. This now varies from round-to-round based on scientific merit relative to those proposals submitted in the thematic areas. Finally, each enabling core is co-led by designated faculty with staff assistance from each institution who are separate from the faculty directing the thematic programs

or the investigators on funded projects. Of the total \$14 M investment, 20% was set aside to fund the cores, travel, and administrative expenses. A decision was made to not invest in buildings or jointly owned structures.

2.3 | Three enabling cores

The Biorepository and Biomedical Informatics Core defines processes by which research data and bio-specimens are collected, stored, and jointly utilized by establishing standardized procedures. Compliance with and adherence to government policies and regulations has been stressed.

The second enabling core, the Institutional Review Board (IRB) and Human Protection Core of the JI, facilitates IRB review and approval processes at each institution. In 2010–11, leaders from the respective institutional IRBs made reciprocal visits and held regular video-conferences to exchange processes and familiarize each other with local rules, regulations, and practices.

The third and perhaps the most instrumental enabling core is the Collaboration Core established to enhance communication, identify opportunities (i.e., connect faculty with mutual interests), optimize the management structure and process to lead to favorable outcomes, and work through problems and barriers as they emerge. The specific work by this core includes facilitation of regular communication through video-conferencing of co-leadership from cores, programs, and projects; management of request for proposals process; assistance with peer review processes for submitted proposals; provision of orientation sessions to new project teams; coordination of reciprocal visits and exchanges, and organization of an annual joint symposium that alternates each fall between PKUHSC and UMMS. Following institutional guidelines and governmental regulations, the Collaboration Core has also been able to facilitate the exchange of biospecimens allowing investigators in select situations to analyze samples collected by their co-investigators in the other country.

2.4 | Research awards

Since January 2011, 10 calls for proposals have been issued soliciting applications for Pilot Awards (funding up to \$800,000 for 2 years) or Discovery Awards (funding up to \$200,000 for 2 years) jointly submitted by faculty of UMMS and PKUHSC. Prior to submitting full proposals, investigators are required to first submit a letter of intent to the Executive Committee that will consider if the concept pertains to diseases of importance to both countries and has the potential to generate pilot data that could be leveraged for external funding. In addition to the original three programmatic themes (i.e., cardiovascular, hepatology/gastroenterology,

and pulmonary), renal disease was added in 2011 because of significant faculty interest at both institutions. In 2012, it was also determined that a limited amount of funding should be set aside for “exploratory areas” outside of these four main programmatic themes. In 2018, Cancer and Precision Health was added as a thematic area.

After the letter-of-intent review, investigators are invited to submit a full proposal, with feedback on how to optimize chances of success, which is evaluated independently by peer review boards facilitated by the Michigan Institute for Clinical and Health Research at UMMS and the Office of Research at PKUHSC where the relative merits are reviewed and constructive comments provided. Investigators then have an opportunity to respond to the comments and improve their proposals before the final ranking is determined by the internal review committees and submitted to the leadership of the Executive Committees for decisions on funding. This requires thoughtful, trusting conversations to reconcile differences in how proposals may be viewed on both sides so as to maximize the quality of the science and its potential impact.

3 | OUTCOMES

Since the first round of request for proposals in February 2011, 190 full proposals were submitted for review of which 59 were selected for funding Table 1. To date, these JI-funded projects have generated 86 peer-reviewed publications that all have a translational science component (i.e., wet-lab or

computational science approaches). In addition to 17 NIH awards, extramural support includes one collaborative award with the NIH Fogarty Chronic Disease Network, and four industry awards for a total of \$5.3 million in U.S. extramural funding. Three patent submissions are underway through Technology Transfer Offices at the respective institutions (targeted imaging of hepatocellular carcinoma, valproic acid for the treatment of myocardial ischemia, and CitH3 in the diagnosis and management of septic shock). Other notable accomplishments include the development of a new specific biomarker in the urine for advancing renal disease,^{9,10} and a body of work on the relationship between air pollution and cardiac disease that has advanced our understanding of disease mechanisms^{11,12} and informed policy discussions at WHO.

Return on investment for the pilot funding allocated is difficult to determine. Follow-on funding in China is more likely to come from institutional “basket” funding from the Chinese government that can be difficult to attribute to a specific project. However, focusing on the U.S. side, extramural funding secured by the UM is \$27,275,313 Table 1 from the actual expenditures of \$8.2 M from pilot funding awarded to the UM investigators resulting in a return of investment of ~230%.

In almost all cases, the investigators had no prior collaborations with each other prior to those facilitated by the JI. It is also worth noting that in 2018 PKUHSC was recognized by the Chinese Ministry of Science and Technology as a National Center for International Research, with UMMS

TABLE 1 Summary of JI funded projects and the outcomes (April 2011 through September 2020)

Thematic programs	No. of Pilot/Discovery Awards	Jl funding ^b	No. of research samples/patients ^c	No. of publications to date ^d	Extramural funding secured—UM ^e	Extramural Funding Secured—PKUHSC
Cardiovascular	9/5	\$6,043,351	19,271	36	\$14,628,096	\$1,045,000
GI/Liver	5/4	\$4,000,174	2749	19	\$4,869,526	\$1,500,000
Renal	2/9	\$2,135,927	110,469	13	\$4,916,944	\$1,242,000
Pulmonary	2/5	\$2,351,963	562	8	\$1,580,747	\$247,000
Cancer	1/1	\$800,000	0	0	0	0
Exploratory ^a	2/14	\$4,389,927	5907	10	\$1,280,000	\$429,000
Total	21/38	\$19,721,342	138,958	86	\$27,275,313	\$4,463,000

Note: Over the past decade, the Joint Institute (JI) for Translational and Clinical Research has supported 59 projects (21 Pilot and 38 Discovery) with total awards of \$19,721,342. The funded studies utilized 138,958 research samples/subjects. The JI work has generated 86 peer-reviewed publications, and extramural funding of \$27,275,313 in the United States and \$4,463,000 in China.

^aThese are areas that were not part of the five thematic programs initially identified as the priorities for the JI, and these exploratory areas include Radiology, Human Genetics, Psychiatry, Emergency Medicine, Obstetrics & Gynecology, Orthopedics, Urology, Dermatology, Dentistry, Rheumatology, Ophthalmology, Neurology, and Surgery.

^bFull awards are for funding up to a total of \$800,000 U.S.; discovery awards are for funding up to a total of

^cWhile the cohort differs for each study, collectively 45% of the patient subjects are from the United States and 55% are from China.

^dSee Appendix I.

^eFunding external to either institution secured with data or activities generated by pilot funding; only United States and international industry sources listed because all funding within China ultimately comes from the government in block allocations.

\$200,000 U.S., with each institution contributing equally to the award; JI: Joint Institute for Translational and Clinical Research.

being Peking University's longest-running and largest international partnership.

4 | A PLATFORM FOR EDUCATION AND TRAINING

The research agendas have provided a collaborative environment for the exchange of students, trainees, staff, and faculty. Some of the exchanges, such as those that occurred with the IRB and Human Protection Core, were critical to the success of understanding UM, PKU, and international practices. Others focused on the need to transfer laboratory practices and policies that were in place at UM to partner labs in China. Of note, China relies more heavily on faculty for research work with little access to clinical research coordinators and program managers that is typical at UM, but the situation in China is improving with the support from the government. Course work and programing was developed to help foster this cohort in China while focusing on skills-transfer to visiting learners from China. Since 2011, 107 faculty or staff from PKUHSC spent time at UMMS for short-term (i.e., <3 months) training and 25 faculty spending time at UMMS for longer-term experiences at times supported by competitive international awards (e.g., Milstein Medical Asian American Partnership Foundation and International Society of nephrology) In addition, a UMMS faculty member was able to successfully secure a Fulbright Award to pursue scholarship in Beijing and four UM faculty to be recognized with "Guest Professor" appointments at PKUHSC.

During this same time period, 15 students from PKUHSC participated in research experiences at UMMS in addition to five who were enrolled in a unique dual M.D./Ph.D. program. Generous philanthropic support from a donor attracted to the JI model of creating mutual benefit between UMMS and PKUHSC resulted in the creation of the Rogel Scholarship Program in 2014, which has allowed five PKUHSC medical students to enroll in the Program in Biomedical Sciences at the University of Michigan Ph.D. programs. These students will graduate with a dual M.D./Ph.D. degree from the respective institutions that optimally prepares them for future collaborative research. Thirteen students from UMMS rotated to PKUHSC for research experiences. These tend to be more short-term rotations (several weeks) when compared to the long-term experiences for those from PKUHSC coming to UM. There are far more PKUHSC learners who speak English and can benefit from a UM experience than there are UM learners who speak Mandarin and could benefit from longer-term immersive experience in Beijing. In addition, learners in China have better access to governmental funding for a research experience at UM than what is currently available for U.S. students seeking longer research experiences in China.

The presence of this platform also facilitated clinical experiences for students wishing to rotate at UMMS from PKUHSC (31 to date) or for medical students/residents to rotate to PKUHSC from UMMS (25 to date). Finally, a yearly 2–3 day joint symposium that alternates between Ann Arbor, MI and Beijing, China now attracts almost 100 visitors from the partner-institution to the host-institution. These symposia focus on information exchange but are crucial to setting the tone for collaboration, finding new partners, and sharing best practices.

In 2017, the JI facilitated an executive education program for one of PKUHSC's main hospitals (i.e., Peking University Third Hospital) with a focus on hospital leadership and management. Given the success of the pilot program and an increasing demand, Michigan Medicine's *Global Executive Education Program* was approved and established by the Dean's office in 2019. Three cohorts of participants were trained and certified from the program in 2019 with requests increasing from other institutions across China.

5 | DISCUSSION

5.1 | Lessons learned and experience gained

The JI has established a culture of collaboration by involving approximately 300 individuals, including faculty, trainees, and students from UMMS and PKUHSC to explore joint research and education opportunities. These individuals represent a majority of academic departments at each institution. Another benefit of the JI has been the ability to attract colleagues from other health science schools including nursing, public health, dentistry, and pharmacy into engagement with JI initiatives. An annual symposium regularly attracts 80–100 visitors from the partner to the host institution. Cooperation has also been carried out in the area of medical education with the exchange of students and trainees.

A number of challenges have been encountered and resolved resulting in numerous "lessons learned." These include the need to carefully evaluate the investigators' readiness to collaborate in addition to assessing the scientific merit of the proposals. High-quality communication also proves to be essential including attention to format (e.g., preference for email by UMMS investigators vs. preference for phone-calls by PKUHSC investigators), as well as optimal communication channels (e.g., more comfort among UMMS investigators in bringing problems forward to leadership relative to their PKUHSC colleagues). Being explicit regarding good communication has been essential for bridging differences in approaches to authorship determination on joint manuscripts. Finally, the ability to obtain proper government approvals for transferring genetic data from PKUHSC to UMMS requires understanding and diligence to ensure that all proper

procedures are followed. Only one approved project has been discontinued because of unresolved challenges mentioned above.

Critical determinants of success include having co-ownership at all levels with co-investment of resources that remain in the respective countries but are mutually determined. It is essential to have a commitment to building trust, working out differences, and ensuring transparency, and a willingness to see good intentions on both sides. The engagement and participation of “boundary spanners”—individuals familiar with the language, culture, and practices of academic communities in China and the United States—has also been instrumental. Of the 10 members on our Executive Board, all from PKUHSC have had training in the United States and none of the 5 from UMMS are native mandarin speakers. Of the 53 co-leads, co-directors, and funded PIs, 52 from PKUHSC have had training in the United States (one at University of Michigan), and 19 out of 64 from UMMS are native mandarin speakers. Lastly, the need to define a communication plan upfront with a process for resolving difficulties that will arise cannot be over emphasized. This is in contrast to approaches that attempt to establish processes when a problem has arisen that is already altering the spirit of the relationships.

5.2 | The value proposition of a JI structure

Collaborative science between China and the United States is well underway, typically driven by faculty who wish to work with each other making use of standard institutional pathways and policies currently in place. The value of a different, often parallel, structure to enable research should be critically evaluated. The key features of the JI that provide added value include:

- Problem solving (e.g., regarding communication, cultural differences); and
- Opportunity seeking (e.g., brokering new partnerships to help investigators find each other and develop new projects, sharing funding opportunities).

An additional value to the JI is the establishment of a continuous, trusting relationship between leadership and faculty at both institutions that can be leveraged when new issues arise outside of the research domains that could benefit from a collaborative approach. One specific example includes how leadership and investigator teams started sharing best practices in the spring of 2020 when the United States was experiencing a surge in cases from the COVID-19 pandemic. A facilitated conference call with teams in Beijing allowed UM faculty to understand best practices to patient-care learned in China that could be applied at the UM before published data were available.

5.3 | Next steps

The JI has already experienced a substantial turn-over in leadership that normally occurs in academic settings, confirming that ongoing success is not dependent on any particular leader or personality. Both institutions expressed confidence in the model by repeating investment of \$7 M from each side for a second 5-year period (2015–20). Joint discussions have resulted in an adjustment to JI strategies such that more emphasis will be placed on disease processes with cross-cutting themes (e.g., metabolism and cancer) rather than the organ-based approaches to building collaborations which characterized the first 10 years. In addition, prioritization will be placed on building high-quality data repositories for partnerships with industry such that private–public partnerships can be a source for ongoing JI funding.

There is a popular Chinese saying “十年磨一剑,” which means “it takes ten years to forge a fine sword.” Over the past decade, the JI’s collaboration platform has been well established. We are optimistic regarding the long-term success of the JI as this model has been deemed valuable by the leadership and the faculty at both institutions. The ultimate test of this model will be the ability to generate new knowledge that will contribute to the health of populations in both countries.

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AUTHOR CONTRIBUTIONS

Joseph Kolars wrote the paper; Qimin Zhan edited the paper.

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APPENDIX I

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