International Medical Research Infrastructure: KUMC and Beyond

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A global research arena has developed since research and education are important to many nations. In fact, many of the rising economies in the world are knowledge-based and thus, technologically oriented. As indicated by Thomas L. Friedman in his book '*The World is Flat: a brief history of the twenty-first century*', the advent of the internet has enabled researchers to communicate without geographic bounds and thus research is no longer geographically restricted. Worldwide research has increased, especially in Asia. Universities world-wide are competing for the same research funds and talented students as well as the same faculty in highly competitive similar disease areas. US universities must have a global presence in order to remain competitive. It is clear that many world wide advanced degree graduates cannot find jobs in their home country. In fact, some graduate schools are less advanced and lack the means for standard evaluation. Funding for research and education are also insufficient, coupled with increased enrollment.

The topic of building academic health center infrastructure worldwide has been recently reviewed by the Association of Academic Health Centers (www.aahcdc.org/policy/meetinghighlights/spring08/index.php) and an International Forum 2008 was held in Washington, DC. In addition, a brief synopsis of global academic health centers was recently published (The Multinational Academic Health Center, AAHC, modified from the presidential address 2007 Spring Dialogues). The following is a summary of those reports.

Benefits

There are several benefits of developing an international research network. The expertise provided by the various partners will allow broadening of the research goals and technologies utilized in the research. Thus, the whole becomes greater than the sum of the parts. Additional benefits include enhancing one's competitiveness for grant opportunities and engaging new students, staff, and faculty with outstanding credentials. For clinical trials, the patient base may be increased.

Recently, Duke University wanted to extend its brand to another part of the world, Singapore's National University, in hope that this would differentiate Duke from other academic health centers and would facilitate some of Duke's research goals. Similarly, the National University was interested in increasing its prestige of academic medicine in Singapore. Thus, they developed the health workforce by specifically increasing the number of physician scientists and physician entrepreneurs in their knowledge-based health care industry. From Duke's view, the National University collaboration provided an opportunity for Duke to experiment with research and educational methods. Duke organized faculty around educational teams and signature research programs in major disease areas. The development of new models at National University allowed transfer of methods back to Duke's program in the US. Other examples, summarized at the AAHC International Forum were international collaborations with individual schools such as Johns Hopkins, Mayo Clinic, University of Toronto, and the University of Pittsburgh.

Basic Principles

International collaborations will enhance discovery, strengthen and protect research programs by integrating basic and clinical research and, where feasible, encourage translational research. One major goal is to establish long lasting relationships with the international collaborators. In establishing international collaborations high standards should be set with a solid vision including short and long term goals. Clear expectations should be evident and solid leadership is also important. The needs of each participant should be delineated and met.

Drug Discovery: Open Source Concept

International collaboration in the drug discovery arena has taken a recent turn as described in an interesting article by Seema Singh in Cell 133, April 18, 2008 entitled: *India Takes an Open Source Approach to Drug Discovery*, which is summarized below. India is launching an open source drug discovery initiative to accelerate development of new drugs to treat infectious diseases of worldwide importance. In addition, there is a need for new low cost drugs. Because drug discovery is so complex and challenging, India is establishing a web-enabled interactive open source platform that will list the current design challenges for developing drugs to treat drug resistant tuberculosis, malaria and HIV. Volunteers contribute solutions to the posted drug design challenges and microcredits are given to the contributors. Once a certain number of microcredits have been accrued, the contributor will receive a monetary award (reward).

Examples

Open source software started 17 years ago by Linus Torvalds, who developed the Linux operating system. Biologists borrowed from the Linux concept and started development of bioinformatics tools such as BioJava, BioSPice, and BioRuby as well as others. The sharing of bioinformatics know-how has paved the way for additional projects. For example, CAMBIA was launched by molecular biologist, Richard Jefferson in Australia as an international nonprofit institute for creating new technologies and tools to enable innovation in health, food security and natural resource management for the developing world. Several spin-off were formed including BIOS (Biological Innovation for Open Society: www.bios.net/daisy/bios/about/3.html), BIOS also developed a gene transfer technology called TransBacter that can be used instead of the costly *Agrobacterium* for genetically engineering plants and Patent Lens (patentlens.net/daisy/patentlens.html) that searchers the full text of over 8 million patents and applications world wide. Patent Lens has a server that extracts DNA, RNA and protein sequences from US patents and links them to GenBank and BLAST searchers. This team is working on launching an international open innovation platform to assist searching patents filed world wide.

Successes

Several examples of open source successes exist. There has been improvement of the drug used to treat schistosomiasis. This required the drug to be enantiopure rather than racemic. Via the web a suggestion was made for the synthesis. The team has taken the suggestion and is in the process of producing the enantiopure drug. Another example includes the drugs to treat malaria. Two compounds are somewhat active against malaria. Three groups across the US participated with one group producing the docking calculations, one group did the synthesis and the other group did the testing.

Innocentive is an open source drug discovery company spun out of Eli Lilly. Users can select an R&D challenge posted by a company or a not-for-profit and attempt to solve the problem for a cash award ranging from $5,000 to $1 million. Among their successes are included new methods to synthesis fluorinated ethers, butanoic acid, and identification of new drug targets for treating Muscular Dystrophy. Currently, there are posted challenges to find a diagnostic biomarker for ALS. Lastly, Novartis has made all information about genes implicated in type 2 diabetes obtained from genome-wide association studies freely available on the web in an effort to speed up elucidation of the mechanisms underlying this complex disease. Harvard and Lund University (Sweden) are participants in this study.

Rationale and Challenges

One might ask: why use open source and what are the associated challenges? First, the goal is to help resolve key scientific and drug discovery problems with multiple inputs thus accelerating drug development/ discovery in specific disease areas. In fact, the European Union's Innovative Medicines Initiative, EU-IMI, a partnership between the European Community and the European Federation of Pharmaceutical Industries and Associations, is addressing this issue also. The open source concept allows investigators to view specific drug discovery problems and pose solutions. Solutions are proposed by individual investigators or teams of investigators from the same or collaborative institutions. One driving force for using open source is that many drug discovery problems are complex, requiring many labs for insights. Several challenges exist such as assigning appropriate credit and ownership of the intellectual property. In addition, the timing of disclosure, protection of the discovering scientist(s), and subsequent product patent filing limitations may all be formidable issues.

KU and Beyond

The KU School of Pharmacy has a high national ranking as evidenced by their continued success with NIH funding, training of students, and the esteemed nature of their faculty. Major strengths are in the areas of Chemical Methodologies Library Design and Drug Discovery, Development and Delivery. KU also has a very solid connection with major pharmaceutical and biotech companies. Currently, Drug Discovery has more than 70 projects in the drug pipeline. This is largely due to their superb organizational structure that includes outstanding high and medium throughput screening facilities which produce numerous leads. In addition, the Office of Therapeutics and Drug Discovery has more than 100 years of pharmaceutical industry experience.

This group is further developing their translational research by securing funding from NIH, foundations, and industry in order to support biomedical and clinical proof of concept development. Whether an open source discovery program would facilitate the movement of drugs through the pipeline is uncertain at this time. However, enhancement of collaborations at the local, national and international levels is critical for future success. KU will need to further establish a system that supports entrepreneurship, rewards faculty for their drug discoveries through a traditional promotion and tenure system, and garners more investment for drug discovery, development and delivery that are all consistent with THE TIME IS NOW: a 10-year vision & strategy to advance the life sciences.