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Meeting Report

First Universities Allied for Essential Medicines (UAEM) Neglected Diseases and Innovation Symposium

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Abstract. Universities Allied for Essential Medicines organized its first Neglected Diseases and Innovation Symposium to address expanding roles of public sector research institutions in innovation in research and development of biomedical technologies for treatment of diseases, particularly neglected tropical diseases. Universities and other public research institutions are increasingly integrated into the pharmaceutical innovation system. Academic entities now routinely undertake robust high-throughput screening and medicinal chemistry research programs to identify lead compounds for small molecule drugs and novel drug targets. Furthermore, product development partnerships are emerging between academic institutions, non-profit entities, and biotechnology and pharmaceutical companies to create diagnostics, therapies, and vaccines for diseases of the poor. With not for profit mission statements, open access publishing standards, open source platforms for data sharing and collaboration, and a shift in focus to more translational research, universities and other public research institutions are well-placed to accelerate development of medical technologies, particularly for neglected tropical diseases.

INTRODUCTION

The symposium was held on November 20, 2010, and included four plenary panels covering key subjects related to public sector research, investment in innovation, and access to technologies for neglected tropical diseases (NTDs). The four panels covered the following topics: (1) the current state of affairs in NTD research and technology transfer at public institutions, including the role of academia in the medical innovation system from an industry perspective; (2) specific strategies and barriers to effective collaborations with product development partnerships (PDPs) and industry; (3) novel funding mechanisms for research and development (R&D) programs, financial resources to sustain NTD research at universities, and new approaches to intellectual property to alter incentives for scientific innovation; and (4) the roles of open access publishing and open source (OS) scientific discovery for neglected infections of poverty. The details of each panel follow.

ACADEMIC RESEARCH AND TECHNOLOGY TRANSFER

This panel introduced the global need for new treatment modalities, diagnostic technologies, and vaccines for NTDs. The panel also summarized current avenues of research in the field at universities and industry views regarding key questions that the public sector may be well-equipped to address. The discussion also focused on tools for bioinformatics and data sharing developed by the National Institutes of Health.

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Gloria Tavera (MD/PhD candidate, Case Western Reserve University School of Medicine) began the symposium by addressing the role of universities in addressing NTDs. She highlighted that the gap in life expectancy between the richest and poorest countries in the last four decades has increased and that this health disparity should be a call to arms for scientists, government leaders, medical product developers, and research trainees.[1] Tavera asserted that because universities have a stated commitment to act in the public interest, students, academics, and university administrators are in a unique and powerful position to call for broader access to university research for low- and middle-income countries and answer research questions that address diseases of the poor. Tavera explained that widespread interest in global health at universities exists but must be harnessed in the form of concrete commitments—by addressing not only the big three (malaria, human immunodeficiency virus/acquired immunodeficiency syndrome [HIV/AIDS], and tuberculosis) but also the NTDs of extreme poverty.[2]

Tavera highlighted that many mainstay treatments for NTDs are toxic, ineffective, and unsuitable for pediatric use. She cited the 2009 G-FINDER Report, which showed that, of the $3 billion US invested in research, only 0.4% was allocated to NTD-related work.[3] She proposed that universities must join the National Institutes of Health (NIH), philanthropic donors, and developing countries in their efforts to increase research in this area. She encouraged universities to harmonize their efforts with NTD networks and global health initiatives for the dual purposes of enhancing awareness of disease-specific needs at the university and bolstering administrative support. Furthermore, she asserted that universities might also raise money for NTD research by creating seed funds in the spirit of existing country-level programs in which 0.7% of national gross domestic products are donated to help reach the Millennium Development Goals. Tavera stated that NTD research training and education should be a priority

that may be actualized through training opportunities such as fellowships, symposia, and research collaborations with PDPs. One example of the pioneers on the NTD front that Tavera mentioned is the Henry Wheeler Center for Emerging and Neglected Diseases at the University of California at Berkeley, which promotes partnerships between the university and the Global South for the development of NTD-related biotechnology.

Tavera also asserted that students must continue to advocate for universities to not only increase their commitments to NTD-related research but also ensure that resulting innovations reach the populations that need them. Academic technology transfer offices can help by implementing equitable technology licensing strategies, including at cost provision or sublicensing terms for resource-limited countries. She described specific guidelines for achieving these goals as outlined by Universities Allied for Essential Medicines (UAEM) in the Global Access Licensing Framework,[4] a document that serves to guide university licensing practices. She added that a consensus document embracing many of these principles was adopted by 26 research institutions including the NIH, the Centers for Disease Control and Prevention, Harvard University, the University of North Carolina at Chapel Hill, and Yale University.[5]

Mukul Ranjan (Chief, Immunology and Emerging Infectious Branch, National Institute of Allergy and Infectious Diseases, Office of Technology Transfer) began the panel by highlighting that the NIH provides 40% of worldwide research funding for NTDs. Ranjan also stressed practices in open access and sharing that extend the funding dollar and create efficiencies that can be leveraged to facilitate NTD research. He outlined strides made by the NIH in open access science, starting with the establishment of GenBank in 1982, which made deposited gene sequences publicly accessible in an open digital repository. Along a similar vein, in 1999, the Research Tools Sharing Policy strongly recommended that NIH-funded investigators share research materials; by 2003, the NIH required grantees awarded greater than $500,000 to provide and enact a data-sharing plan.[6,7] This policy was followed by a model organism sharing policy in 2004.[8] That same year, the NIH launched PubChem, mirroring GenBank, for sharing chemical structures, assays, and assay data. Ranjan noted that NIH public access sharing policy now mandates that manuscripts describing NIH-funded research be deposited into PubMedCentral, a free public repository, within 1 year of publication.[9] He explained that this policy was intended, in part, to enhance access to research by those people in resource-poor countries.

Ranjan shifted focus to the history of drug development. He explained that, previously, large public sector research institutions such as the NIH have traditionally focused on basic research. Therefore, moving basic discoveries forward to drug development depended overwhelmingly on the private sector, motivated essentially by market incentives alone. To preserve projects that often failed in an early phase of development—the so-called valley of death—the NIH Molecular Libraries Initiative assembled compound libraries from academia and the private sector. It began to provide compound screening, protein production, assay development, and robotics facilities.

Ranjan highlighted that the NIH acknowledged the gaps in technologies for rare, orphan, or neglected diseases and therefore, established the Therapeutics for Rare and Neglected Diseases (TRND) Program in 2008 to enable private and public sector investigators to take lead compounds through preclinical testing. The program sought to evaluate five drug candidates every 6 months, allotting $5–10 million to each. Of note, one founding project focused on the NTD schistosomiasis, whereas the other four addressed rare diseases. Furthermore, Ranjan explained that all data and probes generated within TRND must be released to the public domain within 2 months of discovery. At the other end of the drug development pipeline, NIH contributed its intellectual property rights to the HIV drug darunavir to the Medicines Patent Pool, making it the first drug to be added. The Pool brings together patents to provide patients in low- and middle-income countries access to affordable and appropriate drugs.

Ranjan reminded the audience that the National Institute of Allergy and Infectious Diseases (NIAID) is the primary NIH institute that deals with infectious diseases and vaccine development, and it does so by supporting capacity building, training scientists, establishing research sites overseas, and assisting with Food and Drug Administration drug applications. In addition, he emphasized that the institute also maintained clinical trial sites for malaria, HIV, and other diseases and maintains free reagent repositories and support for preclinical animal testing.

Ranjan ended with the most recent open access initiatives at NIAID, which included the establishment of the Human MicroBiome project,[10] the Eukaryotic Pathogen Database,[11] and the Influenza Research Database.[12] Ranjan asserted that in doing so, the NIH recognizes that successful biomedical research will require approaching the massive inflow of data in a systematic way and providing broad access to research tools and ideas.

John Erickson (President and Chief Executive Officer, Sequoia Pharmaceuticals, Inc.) spoke on the potential roles for academia in drug innovation from a private sector standpoint. He believes the primary problem in drug innovation is that the cost for developing drugs for low-paying markets is the same as the cost for high-paying markets, whereas market incentives are much lower for the former. He highlighted that few drugs survive the R&D pipeline and that costs and risks increase dramatically as a drug advances through the stages of development. He stated that universities are uniquely positioned to conduct operational research to improve R&D efficiency and reduce duplication of research, develop tools of pharmacology to better predict parameters such as solubility, and determine safety profiles of compounds at an early stage. He also noted that, for NTDs, more basic parasitology research is needed to identify drug targets and that academia may be able to best address this need.

Several common myths regarding R&D for NTDs need to be debunked, Erickson believed. First, he explained, the retail price of a patented drug is mistakenly thought to be related to its total cost of manufacture. In reality, the retail drug price is driven by market price—how much consumers are willing to pay. Second, Erickson asserted that patents do not necessarily block development of drugs and do provide protection for the investments made during drug development. Third, he argued that development of drugs for NTDs afflicting neglected people was not inherently cheaper. He stated that, in actuality, regulations, safety, and efficacy data requirements incur similar costs for drugs designed for developed and developing countries.

Erickson ended the panel by challenging biotechnology and pharmaceutical industries, academia, and nonprofit entities to develop drugs for neglected people both at home and abroad. He believed that a potential role for the NIH was exemplified by the National Cooperative Drug Discovery Group (NCDDG) for AIDS,[13] which provided multimillion dollar grants to researchers in both public and private domains to collaborate in translating basic research in retrovirology—including new drug targets—into drugs. In doing so, NCDDG succeeded in creating the first pharmaceutical agents active against viruses. Erickson asserted that NCDDG funding also allowed him and others to pursue the development of ritonavir and lopinavir, drugs that remain widely used for HIV treatment. He closed by suggesting that this same model should be applied to NTDs.

UNIVERSITIES, PDPS, AND INDUSTRY COLLABORATIONS

This panel featured leaders from academia and the PDP sector who have partnered with both universities and industry to develop new technologies for leishmaniasis, hookworm, tuberculosis, and malaria. The panel highlighted the role that universities and university students can play in promoting the success of such collaborations.

Kishor Wasan (Cofounder/Director, Neglected Global Diseases Initiative and Professor, Faculty of Pharmaceutical Sciences, University of British Columbia) spoke about working as an academic scientist at the nexus of basic research and drug discovery and the challenges faced in founding the Neglected Global Diseases Initiative at the University of British Columbia (UBC). Wasan presented the following fundamental question: how can universities translate discoveries in the research laboratory to new technologies for the developing world? He emphasized that it is important for global health advocates to think about neglected people, not just neglected diseases, noting that this thought requires a multidisciplinary approach to also address inadequate healthcare delivery infrastructure and poor rates of retention of physicians and medical scientists in developing countries.[14] These problems involve political, economic, and logistical issues. Wasan also highlighted other initiatives at UBC that address global health and development, including the Center for TB Research, the Health Technologies Access Program, the Center for International Child Health, and the Accessible Science Initiative.

Wasan stressed the need for greater funding and university encouragement to do NTD research and creativity in protecting early discoveries to ensure adequate testing of early-stage compounds. He cited his own discovery of the novel lipid-based oral formulation of amphotericin B used to treat visceral leishmaniasis and described its licensing by UBC to iCo Therapeutics.[15] Technology transfer policies in place at UBC ensured that this technology was made available at or below cost in least-developed countries.[16] In parallel, he explained that the drug would be marketed to treat systemic fungal infections in wealthy countries at a higher price. The pragmatic advocacy approach taken by UBC students affiliated with UAEM was crucial to the adoption and successful implementation of the global access technology transfer policy at UBC. Wasan concluded by insisting that such efforts can best succeed at other universities by gaining the support of their most respected researchers.

Rita Khanna (Legal Counsel, Aeras Global Tuberculosis Vaccine Foundation) spoke about university partnerships with PDPs and the challenges faced by Aeras in collaborating with university laboratories and technology transfer offices. She indicated that barriers to the development of vaccines for diseases of poverty, such as tuberculosis (TB), include the lack of vaccine development capacity in developing countries and the low profit margin for most vaccines. The existing Bacillus Calmette-Guérin (BCG) vaccine developed over 80 years ago is not effective in preventing adult pulmonary TB, and it has little to no effect in slowing the global TB epidemic.[17] The goal of Aeras is to have an efficacious TB vaccine on the market within 7–10 years and make it available at affordable cost where it is needed most.

Khanna pointed out that there were more than 300 drugs in development for cancer and fewer than ten for TB in 2006, despite the fact that one-third of the global population is infected with TB and close to 2 million people die annually.[18] To address this gap, PDPs such as Aeras have established a new institutional framework for biomedical R&D to provide products for the developing world at the lowest possible cost. Currently, Aeras is conducting a Phase IIb trial of a candidate TB vaccine at field sites in Africa in an effort involving at least two universities. This trial represents the farthest advance of any TB vaccine candidate in clinical testing since the introduction of BCG vaccine in the 1930s.

Khanna explained that Aeras has collaborations with many organizations in academia, industry, government, and charitable foundations. She emphasized that one barrier to success is the frequent practice in university technology transfer offices that require milestone payments from their PDP collaborators for incremental advances in development of the technology. Such requirements, Khanna stated, confer a heavy administrative and financial burden and consequently, pose a major difficulty for non-profit PDPs like Aeras. She asserted that milestone payments should be waived for licensees developing products for NTDs. Some universities have allowed royalties to be reinvested into future vaccine development and other R&D at Aeras. Furthermore, Khanna called on universities to measure their success based on the global impact of licensed technologies rather than focusing solely on revenue and royalties.

Neeraj Mistry (Managing Director, Global Network for Neglected Tropical Diseases, Sabin Vaccine Institute) spoke about the recent emergence of PDPs as important players in developing new technologies for NTDs. He explained that—unlike researchers working on HIV—those researchers working on NTDs have lacked an empowered community of advocates to drive the research agenda forward. This disadvantage, he asserted, was compounded by the fact that NTDs do not carry the same rates of mortality as do the big three of HIV, TB, and malaria, despite collectively being a major driver behind the loss of global disability-adjusted life years, quality of life, and economic potential.

The Sabin Vaccine Institute was founded with the goal of developing vaccines for NTDs such as hookworm and schistosomiasis. Although industry has played a large role in drug donation campaigns for NTDs, there remains an urgent need for new R&D. He also explained that the mission of Sabin extends beyond vaccine development and deployment efforts

to encompass advocacy and outreach initiatives to guide and support the NTD research agenda. Mistry noted that Sabin also collaborates with the World Health Organization (WHO) to develop regional strategies for NTD control, focusing on horizontal platforms to strengthen health systems. As 501(c)(3) non-profit organizations, PDPs such as Sabin are able to set their agendas based on global need rather than donor and shareholder mandates.

Mistry identified several important building blocks of a successful PDP and movement around NTDs, including strong communication and organization between partners at different institutions and among different sectors. In his opinion, organizations must also have a charismatic champion who can communicate effectively and inspire diverse collaborators, donors, and advocates. At Sabin, this champion is its president, Peter Hotez.

Mistry believes that academic research institutions are ideally placed to serve as incubators of multisector efforts and are natural sites at which new business models and R&D paradigms can be cultivated. With respect to NTDs, universities could be doing more on all these fronts, along with improving and increasing the education that they offer relevant to the field.

Adam Richman (Senior Scientist, Sanaria, Inc.) spoke about the challenges and successes in development of an attenuated vaccine for malaria using parasites irradiated in the early stage of their lifecycle. Sanaria has important collaborations both nationally and internationally with institutions in a variety of sectors. Its funders include the Institute for One World Health (iOWH), Medicines for Malaria Venture (MMV), Program for Appropriate Technology in Health (PATH), the US Department of Defense, and NIAID through the Small Business Innovation Research program.

Richman reported that malaria currently kills nearly 1 million people and causes an estimated $12 billion of lost economic activity each year.[19] Despite significant advances in prevention and treatment, he predicted that an effective prophylactic vaccine would likely be necessary to eliminate malaria in the face of rising drug resistance. Sanaria's stated goal is to create a vaccine that is over 80% effective and delivered to the populations most in need.

Because malaria parasites move from the liver to the blood, Richman explained, blocking the late liver stage of parasitic development would be ideal to prevent progression from the liver to the blood stage and subsequent transmission of the parasite by mosquitoes. This model is unconventional because of the difficulty in manufacturing irradiated parasites in the pre-erythrocyte stage. Richman noted that regulatory challenges arise from the lack of knowledge about the correlation between the animal model and human infection. In 2009, Sanaria submitted an Investigational New Drug application to the Food and Drug Administration for their PfSPZ vaccine candidate based on a non-replicating, attenuated sporozoite stage parasites administered through the intradermal or subcutaneous route. Current efforts focus on optimizing dosing and administration, with the next clinical trial likely to explore intravenous administration. Although the intravenous route presents a significant challenge to access in many endemic regions, Sanaria will likely continue to optimize more feasible dosing routes. Finally, Richman reported that, although the vaccine must be stored in liquid nitrogen (another major barrier in endemic areas), colleagues in Africa are optimistic that these barriers could be overcome if a truly efficacious vaccine were developed.

SUSTAINING RESEARCH WITH EMERGING GLOBAL INNOVATION INCENTIVES AND INTELLECTUAL PROPERTY MODELS

This panel highlighted innovative R&D programs and resources available for universities to finance and sustain NTD research. These resources include innovative approaches to intellectual property that aim to delink R&D financing from profits extracted downstream using proprietary intellectual property frameworks. Both existing and proposed funding mechanisms were discussed.

James Love (Director, Knowledge Ecology International) spoke about new global innovation models and their application to the university context. Many of these models aim to harness the global willingness to pay for R&D as a public good and stimulate innovation while maintaining transparency. Because the global markets offer little commercial incentive for innovators to address some of the world's most pressing health needs, R&D funding should be delinked from the final cost of a product (i.e., high-end product prices should not be prerequisites to funding medicine R&D).[20] Such proposals have been featured in WHO assembly resolutions,[21] but Love claims the rhetoric has been stronger than action. Both push mechanisms—such as grants to fund research—and pull incentives—such as innovation inducement prizes to replace product monopolies—are needed. He provided the following overview of incentives.[22,23]

The FDA seeks to stimulate research on drugs for orphan diseases by providing a 50% tax credit for the cost of clinical trials.[24] Love pointed out that universities are tax-exempt institutions and therefore, not amenable to tax credit incentives. Additional problems with the orphan drug designation, he continued, include a recent elimination of means testing (which helped to avoid exploitation by the innovating company) and lack of transparency regarding the amount of money needed to run a clinical trial.[25,26] Another incentive, the priority review voucher (PRV), is meant to speed approval for future technologies as a reward for developing technologies to treat NTDs; however, this reward can be sought regardless of medical importance of the NTD medicine or whether the drug was already on the market.[27] To date, PRVs have only been granted for products already on the market, and therefore, their ability to spur new innovation is uncertain.[28] Of concern with both the orphan drug designation and the PRV, according to Love, are the lack of standards of transparency and access to the end products of the technology; no access provisions are required, and no mechanism exists to deal with abusive pricing, despite the benefit provided by taxpayers.[29]

Love then described advance market commitment programs and guarantees to buy products at fixed prices to stimulate R&D to address a clinical need. Recent examples include pandemic vaccine supplies,[30,31] especially for pneumococcal disease.[32] According to Love, a market guarantee for the original developer may not be sustainable in the long term and may negatively influence low-cost, local competitive producers. Another concern relating to access is that commitments are made without evaluation of cost/benefit of its exclusivity. Vaccine manufacturers, for example, receive 6 months of exclusivity in pediatric markets in high-income countries,[33] and

no mechanism exists to deal with eventual price increases.[34] Love claimed that advance market commitments also suffer from the common flaws of the orphan drug designation and the PRV: lack of transparency and no incentive to share data, materials, or technology.[35] These flaws could result, among other things, in restricting the number of producers who can ensure supply and generic competition to lower prices.

Love reminded the audience that large philanthropic granting foundations, with the Gates Foundation paramount among these groups, have mobilized enormous resources to address needs of the very poor; consequently, their influence both on global health priorities and access norms is substantial. Because this influence may overshadow the role of public institutions, Love believes it deserves more discussion—in particular, addressing Gates' opposition to the use of compulsory licensing and lack of support for the development of incentive mechanisms based on open licensing mechanisms.[36]

Innovation inducement prizes are a pull incentive that rewards ideas deemed worthy of funding, typically in a competitive process that includes many applicants.[20] Prizes may present more efficient incentives for drug development by enabling crowd-sourcing and rewarding precompetitive R&D. When access strategies are leveraged on the final products of research, they can bring lower prices to consumers of the end products. One example is the OS dividend (OSD), which aims to proportionally reward all contributors to a successful drug development initiative who openly share their databases, libraries, data repositories, and other materials.[37] Academic researchers could choose to partake in the OSD as an alternative, rather than a supplement, to traditional incentives (i.e., payments or royalties based on proprietary or restrictive licensing). The OSD has been included among R&D prize proposals considered by the WHO,[38] and in the United States, this new incentive for openness and sharing has been introduced into the Senate (two bills[21]: S. 1137 and S. 1138) and would involve a portion of domestic drug sales to fund the OSD dividend pool. Among all the mechanisms that he described, Love placed particular emphasis on evaluating implementation strategies for the OSD.

Additional incentives must address access issues in licensing and patenting, proprietary versus restrictive practices, and secretiveness versus sharing in knowledge and research. According to Love, challenges for UAEM and other advocacy groups include setting standards for transparency within the medicines industry regarding scientific, medical, economic, and financial issues, particularly the disclosure of licensing terms. Without transparency, it is difficult to judge whether terms are properly crafted to be effective, pro-health incentives. Furthermore, cost–benefit analyses of incentive programs are crucial to determine best practices.

Paul Wilson (Assistant Professor of Clinical Population and Family Health, Columbia University) spoke on innovative incentive mechanisms, policy measures to solve the problem of R&D for NTDs, and strategies to ensure access to end products.

Wilson noted that the two leading problems in NTD innovation are closely related: the lack of incentives for R&D and price as a barrier to access after drugs are developed. He proposed that the primary existing incentive for commercial investment in pharmaceutical R&D—a partial market monopoly afforded by patent protection—underlies both problems in that the size of the incentive depends not on public health need but on market size, which is almost by definition small for NTDs, and that it works by increasing product prices. Strategies for driving development of health technologies for NTDs must provide an alternative source of funds for R&D.[39]

In general, according to Wilson, incentives for R&D can be divided into two classes: push incentives, which reduce upfront risk and cost, and pull incentives, which increase the reward for successful R&D, supplementing or substituting for market returns.[40] Some new ideas implemented to date include advance market commitments, prizes, and priority review vouchers (pull) as well as grants and other contracts that pay for research and agreements with PDPs that channel grant funding and reduce risk (push).

A major advantage of prizes that Wilson pointed out is to allow for crowd-sourcing, linking funders to those people with workable ideas; this route circumvents a common information asymmetry in which R&D funders do not know who has the best ideas *a priori*.[41] The prize-giving organization does not have to specify the players or the path to the goal but only has to create a large reward and let the market try multiple solutions. When the path to an R&D solution (i.e., a promising drug candidate) and a qualified developer are better known, suggests Wilson, this advantage of prizes is less relevant, and a grant or a more traditional funding mechanism may be more appropriate. Still, one drawback of prizes is that product developers need to be able to raise upfront R&D funding; this requirement almost certainly excludes some innovators with promising ideas.[42]

For academic researchers, Wilson reminded, raising funds to pursue an R&D prize is difficult unless existing grants would cover these costs, which would negate some of the advantages of the prize. Commercial innovators, who can fund R&D from existing revenues or raise venture capital, may be the most promising candidates for prizes. Universities, however, could participate through sponsored research programs and licensing intellectual property to companies pursuing prizes.

Wilson drew attention to his report on prizes for NTD R&D written in collaboration with The Results for Development Institute (R4D).[43] A case study of several prize proposals for TB diagnostics—including one developed in part by Knowledge Ecology International and another designed by the X-Prize Foundation, a prize-creating organization that has managed successful prize contests in other areas of technology—found that prizes likely would be useful in stimulating innovation in this area. The R4D analysis concluded that inclusion of milestone awards, payments for achievement of significant interim steps on the path to an approved product, would make the incentive more attractive to small companies that would not otherwise afford additional R&D.

Wilson left us with a question for additional exploration: the scalability of prizes.[43] Sustaining a stream of innovation for NTDs would require an on-going series of prize contests, each of which would involve substantial investment and expertise to design and manage. This issue may be an argument for integrated prize funds covering a range of products. In either case, a sustainable source of funding will be required.

Paul Converse (Research Associate, Johns Hopkins University School of Medicine) presented on the topic of improving resources within the university for NTDs based on insights from decades of experience in NTD research.

First, Converse addressed generating and sustaining interest for NTD research in the academic community. He noted that the Johns Hopkins University (JHU) Bloomberg School of Public Health—which came to exist during a heyday of research in parasitology, bacteriology, and viral diseases—was originally founded with a Rockefeller Foundation grant to deal with the domestic NTD hookworm, known as Southern laziness.[44] NTD support waned, however, as public perception of infectious diseases as a threat declined into the late 1970s.

The 1980s and the emergence of HIV brought change. After decades of neglect, Converse claimed, the focus within the infectious disease community shifted from hospital-acquired diseases to HIV, NTDs, and other diseases affecting neglected populations. Johns Hopkins University kept pace by launching a certificate course in tropical medicine, a TB center, and a private fund to sponsor travel grants to developing countries. Multiuniversity initiatives began with a consortium of universities addressing HIV launched by universities in Pittsburgh, Chicago, and Los Angeles in collaboration with JHU.

Converse outlined three strategies to mobilize resources for NTD research. First, horizontal sourcing allows piggybacking onto related funding opportunities. For example, his colleagues have tapped into funding from the American Cancer Society to fund research for the NTD schistosomiasis, which can lead to bladder cancer. Second, small funders may lead to unorthodox sources of support, sometimes with unique requirements (such as, Converse recalled anecdotally, translating work into the operational language of the grantor). The Community of Science[45] was pointed out as a useful tool to publicize these opportunities.[46] Third, larger NTD-focused programs, such as the New Aid Foundation,[47] Innocentive,[48] and the Tres Cantos NTD-focused laboratory of GlaxoSmithKline,[49] although new and yet to show their promise, have—in his opinion—begun to show an impressive commitment to open innovation models of collaboration.

Converse also addressed three hurdles in securing NTD research funding. First, academic administrators tend to prefer that faculty seek funding which, like NIH grants, provides support for university overhead costs. Second, granting bodies prefer to fund projects with preliminary data, which is, by definition, often unavailable in NTD research. Converse here provided an anecdotal account of his own arduous journey to finally securing NIH funding.[50] Finally, significant challenges stymie the international collaboration needed to involve disease-endemic areas. Converse spoke from his experience in Ethiopia in the 1980s in a laboratory plagued by brain drain of Ethiopian staff and students. In addition, he bemoaned the difficulty of gathering a critical mass of visiting investigators willing to spend significant time, interact, and collaborate with local scientists. In particular, short-term research stints of 1 week or less were more common but in Converse's opinion, counterproductive.

Sandeep Kishore (MD/PhD Candidate, Weill-Cornell Medical College/The Rockefeller University/Sloan-Kettering Institute) presented reflections on students, NTD research, and community building at a university from his vantage point as a graduate student researcher.

Kishore told a moving personal account of losing a personal mentor to cerebral malaria in India as well as his own bout with the disease with a recovery aided by access to essential medicines. He devoted his PhD to battling NTDs; however, he judges that the current outlook for the current pipeline of academic NTD research trainees is not good. Some university department chairs still do not value global health, and career opportunities seldom reward students' passion and vigor.

To address this problem, Kishore suggests reevaluating academic contributions according to global impact. Complementary metrics for success should consider health outcomes in addition to publications for both tenure decisions and postgraduate student progression requirements. He encouraged students to take the lead when possible. As an example, Kishore described how he successfully lobbied his graduate program to waive one-half of his graduation course requirements in recognition of his work, categorized as independent study, in service to the UAEM Board of Directors and the WHO Essential Medicines List. Meanwhile, unaffiliated global health experts can move to influence academia by seeking adjunct professor status at universities to help facilitate engagement with the next generation of NTD leaders.

Education sensitizes trainees to issues of global health and NTDs. At Cornell, a large medical campus event featuring global health leaders drew an audience of hundreds and left a lasting influence, garnering the support of both the Dean of Medicine and the University President. After the event, the student organizers developed an elective course in global health at the behest of medical school administrators. The course spanned health economics, basic science, clinical medicine, nutrition, and population health and was attended by an impressive 30% of the medical school class.

The curriculum should also focus on interplay of poverty and NTDs with chronic and noncommunicable diseases, such as cardiovascular disease, depression, asthma, cancer, and even injury. Classifications of diseases as infectious or noncommunicable are limiting, because illnesses influence each other. The NTD Chagas disease is a driver of cardiac myopathy, for instance, and schistosomiasis pre-disposes to bladder cancer. Conversely, noncommunicable diseases such as diabetes can pre-dispose a patient to acquiring an infectious disease. Furthermore, such risk factors as tobacco use negatively affect health outcomes for patients regardless of the disease etiology. At universities, such considerations should influence both the clinic and the research laboratory. The Molecules to Humankind PhD program at Emory, for example, combines laboratory and population sciences.[51] To accomplish this task at other institutions, Kishore ventured, would require a fundamental shift in an academic culture that may view population science as less rigorous.

Kishore also spoke of working together with students in the Global South. He spoke glowingly of communications with his UAEM colleague Evance Mbando, who runs the first student-led non-governmental organization (NGO) focused on NTDs in Tanzania at Weill Bugando, a medical college affiliated with Cornell. Institutions; also, individuals can help spread knowledge and models for activism, he stressed, citing the Cornell-Groupe Haitien d'Etude du Sarcome de Kaposi et des Infection Opportunistes partnership in Haiti as additional evidence.

OS INITIATIVES

This panel explored the role of OS initiatives and open access (OA) publishing for university- and government-funded research to address global access to information and its applications to solving public health problems.

Heather Joseph (Executive Director, Scholarly Publishing and Academic Resources Coalition) opened the panel by defining the mission of scientific research as stimulating novel discoveries to influence how people within society think and interact with the world. She argued that the communication of research is, therefore, inseparable from the need to conduct research itself. Furthermore, she asserted that OA publication of scientific discovery should be the norm, not the alternative.

Joseph noted that research communications take place primarily through scholarly journals, most of which are not widely available. She posed that the single greatest barrier to OA publication is cost. One year of leased online access to a journal often exceeds tens of thousands of US dollars annually. She argued that even the best-funded libraries, such as the library at the Massachusetts Institute of Technology, do not have the financial resources available to subscribe to the breadth of journals necessary to conduct research effectively.

Joseph acknowledged that barriers exist, in part, because the academic science publishing industry is lucrative. In 2008, science, technology, and medical journal revenues approximated $8 billion. Although she asserted that price was the main obstacle to the implementation of OA publishing, the explosion of information in the last decade played a role as well, because the scientific community was still developing the technological resources to process exponentially increasing amounts of information.

Joseph stated that OA journals are relatively new and need time and support to become established and respected within the scientific community. Furthermore, she reasoned that business models for OA journals require testing and refinement, whereas cultural change is also required within the scientific community. She believes that the current emphasis on effective communication of scientific findings and viewing published results is insufficient. To enable this shift to take place, she believes authors need training on copyright practices to allow them to make rational choices regarding restrictions versus non-restrictions for their protected information. The Creative Commons set of licenses could be substituted for traditional copyright agreements.[52]

In line with this principle, Joseph explained that universities were using collective bargaining power to challenge exclusive copyright of publishers. Harvard, for example, retained nonexclusive worldwide distribution rights to place articles published by its researchers in an OA online digital repository. Finally, she closed with the assertion that a universal definition of OA methods is urgently needed and offered the following: "The right to access information freely on the Internet and a legal right to interact with material in a robust way."

Zakir Thomas (Project Director, Open Source Drug Discovery [OSDD]) spoke on the initiative established by the Indian Council of Scientific and Industrial Research and funded by a $45 million US grant from the Indian government.[53] Its aim is to foster innovation in a process-driven manner, with OS methods used to avoid encumbrance by traditional intellectual property approaches.[54] The Indian government chose to begin the initiative with a TB project because of the large disease burden in India. Two deaths caused by TB occur in India every 3 minutes, and the global TB drug market is $300 million, an insufficient amount to offset the risk of traditional drug development. OSDD sought to harness OS resources for a small-molecule open repository to allow academics to contribute compounds.

A proof of concept project took place, with a team of scientists in collaboration with students annotating the entire genome of *Mycobacterium tuberculosis* in 6 months. In that time, volunteers made custom database formats to allow interoperability, and most work was done by online collaboration. Students who contributed significantly were made authors. A self-organized hierarchy of scientific discovery emerged: in some cases, graduate students were leading group tasks online, whereas faculty members were group members. This online community annotated and self-corrected the entire genome by December of 2009 by contributing approximately 300 man-years within a 4-month period. Additional OSDD projects will be funded after peer review, with funds dispersed within 30 days to streamline grant reviews and the award allocation process. The OSDD initiative currently has 4,500 members from more than 130 countries.

Rebecca Goulding (ISIS Research Center, Sauder School of Business, University of British Columbia) outlined open innovation in NTD research, noting that this particular area of R&D uses innovative intellectual property strategies to achieve goals of discovery and improve access to these discoveries. For example, an OS-style approach is used by Sage BioNetworks to integrate and share genomic and clinical data that can be used by a large community of researchers to build bionetwork models of disease for drug target discovery.[55]

The concept of OS arose from the free software movement, which developed the General Public License (GPL) to allow users to access and make improvements to copyrighted source code and openly redistribute the improved version.[56] The GPL approach, therefore, reverses intellectual property protection (copyright is automatic) by imposing a copyleft license. In return, the GPL requires that the modified source code of subsequent versions be distributed under the same GPL terms. This viral aspect of OS licenses acts to socially engineer desirable collaborative outcomes by requiring additional sharing of software improvements. Commercially, the OS software business model often relies on the sale of services associated with the software.

Adaptation of OS to biotechnology/biomedicine has been explored in depth by a number of scholars and has been tested by a number of initiatives, including BiOS/Cambia,[57,58] Open Source Drug Discovery,[59] and the Tropical Disease Initiative.[60,61] OS in biomedicine could take different forms, with either a viral license or an academic license that has few impositions other than to protect the original shared data or patented invention. A potential business model for OS in biomedicine could incorporate a value-added, service-based approach like in the OS software industry, although this approach would need tailoring to each invention in question. The use of viral terms, however, may not be applicable for some inventions such as drug targets and compounds, because OS requirements of this nature may dissuade R&D investment, which is currently based on strong IP protection and market monopoly models.[62]

Mat Todd (Cofounder, Synaptic Leap; School of Chemistry, The University of Sydney, Australia) described an OS scientific community collaborative that aimed to address difficult problems in biomedical research.

In January of 2007, the WHO approached Todd to synthesize a low-cost, more pure version of praziquantel, the mainstay therapy for treating the NTD schistosomiasis. The presently manufactured form of praziquantel is a chemical mixture with a bitter taste, leading to dosing limitations and

medication adherence difficulties, particularly among pediatric patients.

Todd emphasized that financial incentives to improve existing drugs are limited. Furthermore, he explained that drugs used to treat diseases primarily affecting marginalized populations have a limited commercial market, which adds another dimension of complexity to an already difficult task. He noted that improved formulations must also have a low cost of manufacture to attract drug companies serving low- and middle-income countries. With these challenges in mind, Todd and colleagues founded the website The Synaptic Leap. At the time, publishing raw experimental data online was rare and in mainstream sciences such as organic chemistry, is not common practice. The Synaptic Leap project received a 3-year $350,000 grant from the WHO and the Australian government to create methods for collaborating on data in experimental science.

The praziquantel chemistry problem is academically challenging and too complex for a single laboratory or researcher to solve within a reasonable time frame. With an open collaborative framework in place, multiple companies contributed to the project, including Dutch-based Syncom B.V.[63] A major benefit of open science was realized: transparency of all data permitted accountability to fellow researchers and the public, the funder behind much academic research. Furthermore, by allowing any individual or entity to contribute to the project and giving appropriate incentives/credit, the problem is potentially attractive in the academic and commercial sectors.

In retrospect, the commercial sector made the most significant contributions to the project. Their help likely arose from company and individual investigator pride, the good public relations opportunity, and the open problem that most have a genuine interest in solving. Improved software is needed to make online collaboration as effective as communicating in person. Universities have been hesitant to buy into this structure. Reward incentives in academia tend to reward high-impact journal publications, and many academic journals do not accept scientific results communicated in the public domain before formal publication, although some reputable journals (e.g., those published by *PLoS* and *BioMedCentral*) have begun to reverse this policy.

Ultimately, Todd reported that the OS collaborative effort was a success. The research was accelerated, because it was OS—people unknown to the team at the outset of the project spontaneously contributed expertise. With major contributions from industry, a novel solution to the preparation of the drug has been proposed that may revolutionize treatment of the 200 million people with schistosomiasis.

TABLE 1

What are the most effective roles for universities and public research institutions in biomedical innovation, particularly for NTDs?

Roles
Support equitable access to biomedical products developed at universities and public research institutions, including medicines, diagnostics, and vaccines
Promote OS science and non-market–driven, need-based research
Ensure the sustainability of neglected diseases research programs with supportive research budgets
Rethink the goals of technology commercialization to focus on access rather than financial revenues
Develop an outcome metrics system to appraise the public benefit of research conducted
Examine tenure track methodologies to ensure that they do not indirectly discourage NTD research, particularly among young scholars
Improve the risk to benefit ratio for young scientists to pursue the field of NTD research
Strengthen the Statement of Principles and Strategies and encourage its use in technology transfer agreements
Promote innovative policy ideas such as prize funds and OSDs and integrate these ideas with current technology transfer practices

TABLE 2

For public research institutions, what are the best practices to use to advance NTD innovation?

Best practices
Improve transparency in licensing terms
Minimize milestone payment fees for licensing of technologies related to NTDs or in instances when doing so could be detrimental for non-profit research institutions
Invest transferred technology licensing royalties back in funding NTD research
Highlight the successes and failures of NTD research to major R&D stakeholders, including the general public and funding entities
Promote non-patent methods to transfer technology when appropriate, which may reduce market costs of the technology
Use open licensing clauses to allow for sublicensing or at-cost provisions whenever possible

CONCLUSION

The symposium ended with an open discussion of future policy directions and advocacy to most effectively leverage university resources, including scientific information, to enhance scientific innovation, particularly for NTDs. Tables 1 and 2 highlight the consensus reached among symposium participants on questions regarding the role of public sector research institutions in advancing NTD research.

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