

## PARTNERSHIPS

# Advancing Translational Research Collaborations

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**In February 2010, the U.S. National Institutes of Health (NIH) sponsored a national Clinical and Translational Science Awards forum titled “Promoting Efficient and Effective Collaborations among Academia, Government and Industry.” This forum brought together a broad set of stakeholders who were charged with developing a path for promoting such partnerships. Here, we describe key issues discussed at the forum and plans for moving forward with this ambitious agenda.**

Although the U.S. National Institutes of Health (NIH) and other academic research centers have made great strides in understanding disease mechanisms, there have not been commensurate gains in new disease treatments, diagnostics, and prevention strategies. One way to address this limitation is through the establishment of alliances among various groups with different strengths and viewpoints who seek to translate basic biomedical research into improved clinical medicine. In order to drive such collaborative efforts, the National Center for Research Resources (NCRR) at NIH sponsored a national Clinical and Translational Science Awards (CTSA) forum that brought together leaders from academia, industry, and government. The forum, which took place in February 2010, was titled “Promoting Efficient and Effective Collaborations among Academia, Government and Industry.” In this Commentary and five accompanying meeting reports (1–5), we describe the key issues discussed at the forum as well as action items that stemmed from this energetic meeting of minds (Fig. 1).

## THE CTSA CONSORTIUM

Until recently, basic research institutions and individual researchers had few incentives to move outside their comfort zones in order to advance their discoveries toward clinical application. To do so means tackling complex clinical discovery and devel-

opment processes, which include new kinds of decision-making models and funding regimens as well as regulatory and patent issues that most basic researchers are not accustomed to handling. When Elias Zerhouni became NIH director in 2002, “that’s the situation as I found it,” he said. “There was a widening gap between basic and clinical research, which if left alone would have been a major barrier to progress” (6). This gap in time, technical capability, and funding between basic discovery research and the application of new knowledge to patient

care is a chasm that has come to be known as the “Valley of Death.”

To address this gap, in 2006 NIH established the CTSA program, which has created a definable academic home to address both the translation of basic science to clinical therapeutics and the translation of therapeutic discoveries to actual clinical practice. All CTSA awardees together form a consortium funded by the NCRR at NIH. When fully implemented in 2012, the consortium will be composed of 60 institutions, with total annual funding of ~\$500 million.

The CTSA Consortium goals are (i) to solve complex problems in medical research by supplying cost-effective research support, such as bioinformatics; (ii) to encourage the career development of investigators interested in translational research; (iii) to work collaboratively so as to improve and reengineer the clinical research enterprise; (iv) to foster innovation through approaches to clinical and translational research; and (v) to maximize results by partnering with for-profit and nonprofit institutions in order to advance medical discoveries (7). These goals are supported by the CTSA Key Function Committees (KFCs) organized by the consortium. KFCs also serve as a venue for sharing best prac-



**Fig. 1. Building bridges.** Distinguished panelists give their 30,000-foot views on future opportunities and unmet needs in translational research. From right to left: Terry Fadem, managing director of corporate alliances for the University of Pennsylvania; Evan Loh, senior vice president of biopharmaceuticals development and strategic operations, Pfizer, Inc.; William New, The Novartis Group; Janet Woodcock, director, Center for Drug Evaluation and Research; Barry Collier, vice president of medical affairs and physician-in-chief, The Rockefeller University; David Kendall, chief scientific and medical officer, American Diabetes Association; and Elizabeth Stoner, managing director, MPM Capital.

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tices and ideas among members in order to carry out consortium projects.

The Public-Private Partnerships (PPP) Committee, one of the CTSA KFCs, was established to catalyze the bringing together of all stakeholders—government, industry, academia, and nonprofit foundations—to accelerate the translation of discoveries through the development process and into commercially beneficial therapies, diagnostics, and devices. The PPP Committee aims to (i) share best practices for technology transfer and research materials transfer across the CTSA, (ii) identify NIH programs that help initiate collaborations, and (iii) provide assistance by identifying opportunities for collaboration and new partnership models to aid in translation.

### THE FORUM: ALL TOGETHER NOW

*Urging participants to “think boldly” about improving collaborative research processes, NIH director Dr. Francis Collins opened the CTSA Industry Forum by commenting on what it will take for the biomedical research community to cross the Valley of Death. “If there are barriers getting in the way of partnerships,” he said, “let’s identify them and see what we can do about them” (8).*

Unlike other similarly conceived events, the CTSA Industry Forum (9) entailed much more than NIH and the CTSA institutions simply declaring, “We are here to partner.” The CTSA PPP Committee organized the forum in collaboration with subject-matter experts from the CTSA, industry, and selected institutes of NIH. Working together, these three stakeholders planned this event by modeling the collaborations they desired to create. The primary purpose of the forum was to initiate a national dialogue to expose barriers to translational research collaborations among government, academia, and industry. The plan was to engage all facets of the continuum, from NIH and the U.S. Food and Drug Administration (FDA) to academic institutions, from the venture capital community to various life science companies engaged in commercial development, and from nonprofit foundations to patient advocacy groups. The resulting forum was proof that all of the stakeholders share a common goal in improving the nation’s translational research infrastructure.

This two-day event brought together more than 600 stakeholder representatives to discuss three key questions: (i) How can

the CTSA program be leveraged to accelerate the discovery and development of commercially viable therapeutics, medical devices, and diagnostics? (ii) What are the challenges and barriers to improving the productivity and efficiency of commercially meaningful translational research? (iii) How can NIH, the CTSA institutions, private industry, and nonprofit organizations work together to address these challenges and barriers?

NIH Director Francis Collins began the meeting by providing NIH’s perspective on translational research and how the CTSA Consortium can begin to bridge the Valley of Death between research discoveries and medical treatments. He spoke of existing collaborations between stakeholders, including the NIH Chemical Genomics Center and the National Human Genome Research Institute’s (NHGRI) Therapeutics for Rare and Neglected Diseases (TRND) program. Through this latter initiative, academic researchers can reduce the risk associated with translational medicine projects by advancing research to the point at which a compound is licensable and an industrial partner can move it forward.

The forum also featured plenary sessions that provided a high-level strategic view of collaboration. One central idea discussed was that collaborations should focus on the systems biology of a potential new treatment in order to understand how a therapeutic target, normal physiological pathways, and disease processes are integrated. Industry “tried to industrialize this space of moving from the lab into the clinic, and we failed,” said Pfizer’s senior vice president of biopharmaceutical development and strategic operations, Evan Loh. “Now what we’re doing on the industry side is asking ourselves, do we really understand the biology?” (10). Industry scientists have realized that they need to reexamine their current drug development methods and find ways of identifying winning compounds earlier in the discovery-development process—and that intimately understanding systems biology is the cornerstone for more efficient development.

The importance of regulatory science came up repeatedly during the forum. FDA’s Janet Woodcock spoke about the difficulty of getting a new drug, biologic, or device to market, because the public expects substantial evidence of the product’s safety and efficacy and has a low tolerance for risk. She also called for data-sharing in toxicology because this kind of information on a particular innovation can provide addi-

tional insight into safety, beyond the clinical reports obtained from patient trials. Gail Cassell of Eli Lilly and Company urged the audience to advocate for more funding for FDA to meet its research mission.

The conference also featured breakout sessions focused on key thematic areas. The intent of these smaller sessions was to stimulate deeper discussions on barriers to collaboration between stakeholders, which could then spawn enduring work streams to make progress on the identified barriers and opportunities. Meeting reports of these breakout sessions can be found in (1–5).

### COLLABORATE TO INNOVATE

Collaboration among all stakeholders in translational research is vital for its success. Examples of fruitful collaborations resonated throughout the event. One of those highlighted was the CTSA Pharmaceutical Assets Portal (11), led by the CTSA at the University of California, Davis, which matches investigators with pharmaceutical compounds that are not being actively developed and can be repurposed for other indications, such as rare diseases. The portal has received a great deal of interest from both academic researchers and pharmaceutical companies, demonstrating the potential to find, through collaboration, new uses for compounds whose commercial development for the initial indication has previously been stopped. A forum breakout session discussed other CTSA-developed by-products that facilitate collaboration (2).

Forum participants agreed that industry and academia can collaborate effectively only when goals, interests, investments, and timelines are aligned. Industry usually makes investment decisions on the basis of the goal of generating commercially viable products. Such decisions are made at each stage of development in a relatively short period of time when one has limited experience with the product, and they attempt to balance development time, benefit, risk investment, and chance of success. In comparison, academic research is usually focused on generating new insights and delving deeply into intricacies of biological mechanisms. This deep experience of academic partners may improve the insight brought to the investment decision-making process (1, 3, 5). If CTSA institutions and industry could achieve agreement on goals for collaborative research, on criteria for research investment, and on timelines to measure progress, collaboration would come more

naturally. Other concepts that were explored included having common agreement templates shared by all stakeholders and finding a project “champion” within the company who will help build and maintain industry-academic collaborations.

Many members of the CTSA Consortium, together with participants from industry, government, and nonprofit organizations, described their desire to lead the change in how clinical and translational research is conducted to improve the public’s health. CTSA investigators discussed how the CTSA program has led to rapid growth in academic translational research in their institutions. However, there was also a general recognition that more formalized structures are needed to ensure sustainable growth of translational research. All parties agreed that there is a need to consider flexible and nontraditional approaches to collaboration, such as pre-intellectual property (IP) partnering, developing multicompany and multiacademic center consortia, licensing to academia from industry, and risk-and-reward sharing. The improvement of translational training and standardization of key translational processes were needs identified.

### EDUCATION AND SHARING

CTSAs are playing a large role in training the translational researcher and clinician. Breaking down of knowledge silos through an emphasis on teaching team science is one of the main goals of the CTSA program. Many CTSA institutions see great value in working with industry to exchange curricula to enhance the training and education of the translational researcher and clinician.

One of the main observations made during the forum was that academic researchers lack a realistic understanding of how new drugs and devices are brought to market. NCR Director Barbara Alving believes that with education, many erroneous perceptions can be addressed. As part of the CTSA program, she said, “a card carrying cardiologist or biochemist or dentist or nurse can have those degrees but also take courses in clinical and translational research” (12). A variety of forum participants characterized the opportunity for industry and academia to work together in training and educating the next generation of translational researchers as “low hanging fruit.”

This topic was discussed with greater specificity during the educational breakout session (4), in which stakeholders shared

examples of exchanges of educational curricula in translational research. For example, Merck, in close collaboration with the Columbia University CTSA institute, has developed a very popular drug development course. There are many examples of such local collaborative efforts throughout the CTSA institutes. However, although these academic entities are well equipped to conduct training in clinical and translational research, this new expertise must be integrated into academic career structures in order to maximally enhance research translation and ensure career advancement.

Furthermore, because one of the CTSA program goals is to encourage public-private partnerships, the CTSA institutes need to consider the cataloging and sharing of large-scale research infrastructures and resources that aid in conducting translational research and clinical trials. Clay Johnston, principal investigator of the University of California, San Francisco, CTSA, suggested, that the CTSA recipients can serve as concierges to facilitate communication and successful interaction among all stakeholders. These institutes can fill a major need in the market by playing an active role with stakeholders to improve their translational research infrastructure. This includes improving business practices, standardizing institutional review board practices, reducing universities’ obsession with IP, increasing flexibility with data sharing, and reducing conflicts of interest. Such efforts could help streamline and reduce the cost of clinical studies and clarify the roles of key players in the enterprise.

During the breakout session on issues and barriers in diagnostic development (1), the NIH Biomarkers Consortium was discussed as an example of an approach that can be taken to achieve improved outcomes (13). It was defined as a model in which industry, academia, and government have worked together to confront thorny issues openly and transparently.

### CLINICAL RESEARCH

If there was one issue that both academia and industry could agree on, it was that little funding exists to support early proof-of-concept (POC) studies, including first-in-human clinical studies. This is a serious problem in translational research, and if the Valley of Death is to be effectively crossed, this funding gap must be addressed. Investigators are hard pressed to find funding for these initial studies, for which the probability

of long-term success is low. Increased POC funding would help produce scientific evidence that exploration of an idea may be feasible in the clinical environment. Small Business Innovation Research (SBIR) funding is one NIH granting mechanism for translational research that is focused on research and development with the ultimate goal of commercialization. Although SBIR applications formally do not require preliminary data, most applicants want to include them because they believe the NIH peer review system will reward it. Although this makes sense as a way to dispense taxpayer funds, it also leaves us without many mechanisms to fund innovation. Earlier this year, the White House Office of Science and Technology Policy and the National Economic Council issued a Request for Information (RFI) on POC centers as they search for promising practices and successful models for fostering commercialization and diffusion of university research (14). Information from this RFI will be used to shape the Obama Administration’s future policy on the commercialization of federally funded research.

During the forum breakout session on the issues and barriers in device development (5), there was a strong consensus among the session participants that it is crucial to create mechanisms to quickly evaluate and approve pre-SBIR-type grants for POC projects. Although many CTSA institutions have implemented small-scale POC awards, the funding gap on a national level remains between basic research discoveries and feasibility studies that could help identify commercial potential. Compounding this already debilitating situation is the realization that both industry strategic partners and the VC community prefer to invest at a later, less risky development stage, when there is more evidence of the probability of commercial success.

The crucial role of nongovernmental organizations (NGOs), such as patient advocacy groups and disease-focused foundations, in delivering POC resources was also highlighted at the forum. During the breakout session on drug development (3), participants revisited the history of the development process for TOBI (Tobramycin Inhalation Solution), a prescription inhaled medication for cystic fibrosis (CF) patients. Panelists discussed how venture philanthropy from the CF Foundation was crucial in helping to fill the funding and resource gap between basic research and phase III clinical studies. Although the CF Founda-

tion involvement was viewed by some as a nontraditional means to a desired end, this foundation's support and the resulting orphan drug status were effective in enticing a corporate partner to further develop TOBI as a commercial product.

### END OF THE BEGINNING

The CTSA Industry Forum successfully opened a national dialogue focused on building more effective collaborations in translational research in order to bring safe and effective treatments to patients. This event was an important first step to address the challenges now facing the translational research enterprise. Forum attendees agreed that the CTSA Consortium infrastructure is well positioned to serve as a vehicle for testing new initiatives designed to drive translation. Rapid and efficient progress on all fronts will require close coordination and collaboration among stakeholders. To be truly effective in confronting the challenges that currently face translational medicine, participants agreed that the dialogue among academia, government, and industry begun at this forum must now be set into action.

Indeed, the CTSA Industry Forum's planning team will transition into a strategic oversight team that has agreed to accept the responsibility for continuing the dialogue so as to promote the forum's recommendations on overcoming the barriers facing translational research.

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