Translational Research: Moving Discovery to Practice

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In the first week of October, I announced the launch of a national consortium that will transform how clinical and translational research is conducted; ultimately enabling researchers to provide new treatments more efficiently and quickly to patients. This new consortium, funded through Clinical and Translational Science Awards (CTSAs), begins with 12 academic health centers (AHCs) located throughout the nation. An additional 52 AHCs are receiving planning grants to help them prepare to apply for a CTSA.

When fully implemented in 2012, about 60 institutions will be linked together to energize the discipline of clinical and translational science. The development of this consortium represents the first systematic change in our approach to clinical research in 50 years. Working together, these sites will serve as discovery engines that will improve medical care by applying new scientific advances to real-world practice. We expect to see new approaches reach underserved populations, local community organizations, and health-care providers to ensure that medical advances are reaching the people who need them.

In a second historic announcement, the Foundation for the National Institutes of Health (FNIH), the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Pharmaceutical Research and Manufacturers of America (PhRMA) announced the start of a major public–private biomedical research partnership, *The Biomarkers Consortium*, to search for and validate new biological markers (biomarkers) to accelerate dramatically the delivery of successful new technologies, medicines, and therapies for prevention, early detection, diagnosis, and treatment of disease.

The utilization of biomarkers, which are the molecular, biological, or physical characteristics that indicate a specific underlying physiologic state, has already had an immense impact upon the prevention and treatment of disease. For example, blood pressure and cholesterol biomarkers have enabled diagnostics and therapies that have contributed to a 50 percent decrease in cardiovascular mortality in the US over the past 30 years.

We are also striving to build powerful, new scientific resources for the research community. One such example is a new proposal to create a genotype–phenotype database for all of the NIH-supported genome-wide association studies. Through this effort, we hope to establish a common data repository at the NIH to promote and facilitate the widespread sharing of genotype and phenotype data as well as the significant associations between them. Because the proposed database would contain data sets from many studies, it would facilitate broader secondary analysis and therefore enable many more scientific inquiries to be pursued at the same time than could otherwise be accomplished currently. As a result of the more rapid analysis and identification of genetic contributions to diseases and medical conditions that will be possible, we will be better able to accelerate the design of improved diagnostic tools and to develop new, safe, and effective treatments.

The NIH is dedicated to improving medical research in ways that will benefit the researcher, the institutions conducting the research, and the public. To address the challenges that researchers encounter, NIH developed a series of initiatives, collectively known as the NIH Roadmap for Medical Research (http://nihroadmap.nih.gov/). The NIH Roadmap, which is the result of ongoing consultations with scientists and clinicians, charged with thinking broadly about the future, has three themes: New Pathways to Discovery, Research Teams of the Future, and Re-engineering the Clinical Research Enterprise. The Clinical and Translational Science Awards (CTSA) program is the result of the creative thought that focused on re-engineering clinical research. Additional specific initiatives address research training that applies to clinical, translational, and interdisciplinary research. In fiscal year 2006, Roadmap funds comprised 1.2 percent of the total agency budget.

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Roadmap funds are generated through budget-proportional contributions from individual NIH Institutes and Centers. Since the inception of the Roadmap program, NIH has funded 379 new awards, which were distributed to 308 investigators at 134 institutions in 33 states. Of these investigators, 56 were new to NIH funding. Roadmap funding was highly competitive, with Roadmap success rates for fiscal year 2004 and fiscal year 2005 at 13.2 and 17.2 percent, respectively.

Speeding translation requires a steady pipeline of clinical and translational researchers; interdisciplinary teams that can collaborate with federal, industrial, and community partners; and integrated resources and informatics to achieve cost efficiencies that will yield new products, approaches, and diagnostic tools in less time. Through the CTSA program, awards will support two critical areas of translational research. One is the process of applying discoveries generated during laboratory research and in preclinical studies to the development of trials and studies in humans. The second area of translation concerns research aimed at enhancing the adoption of best practices in the community. Through these awards, academic health centers (AHCs) across the country will create individualized academic "homes" for clinical and translational science.

Such "homes" will give institutions unprecedented flexibility to design their own programs and develop a center, department, or institute of clinical and translational science. With particular emphasis placed on creating graduate degree-granting and postgraduate programs in clinical and translational science, we expect to see an enriched environment for educating and retaining the next generation of clinical and translational researchers. To encourage interdisciplinary team science, the CTSA program will train investigators from the diverse disciplines required for effective translational research. Training researchers in clinical and translational sciences who have such varied expertise should yield truly novel approaches to and methodologies for conducting research.

CTSA institutions will work as part of a national effort to expand and improve clinical research informatics to share data across disciplines and across institutions. Health information technology (IT) is a complex, critical, and costly issue not only for medical research but also for the entirety of the health-care sector. The Office of the National Coordinator for Health Information Technology at the Department of Health and Human Services provides leadership for the development and nationwide implementation of an interoperable health IT infrastructure to improve the quality and efficiency of health care and the ability of consumers to manage their care and safety. Although the needs that permeate the entire health-care IT sector transcend NIH's purview, we can and are contributing to building and linking clinical research informatics networks. Over time, such research networks could reduce costs, startup time, and duplication, and increase public awareness and participation in clinical research. We can also explore ways to enhance researchers' and regulatory organizations' access to clinical research data. These opportunities, although exciting, still need much more consideration with regard to protecting patient confidentiality and ensuring data validation.[1]

New and expanded IT will help to solve issues related to workflow, usability, and interoperability with collaborating organizations, along with the need to ensure privacy and confidentiality of human subjects. The CTSA program will support the development of such innovations at the institutional level and will create a nationwide consortium where all CTSA institutions will collaborate to develop standards, best practices, and solutions to informatics-related problems.

The CTSA program will not only translate basic discoveries into the clinic, but also further translate and disseminate new findings into real-world practice. Therefore, CTSA institutions will have strong links to the public and local communities. The flexibility of the CTSA program provides opportunities for creating two-way synergies with local and regional communities by reaching out to underserved populations, community-based groups, and health-care providers. In return for the community's participation, the CTSAs will help to deliver improved medical care to the entire population, helping to disseminate new technologies and new advances into clinical practice. Partnerships with industry will also be crucial to moving discoveries to the clinic and beyond as new drugs or new uses of approved drugs are developed.

However, the impact of the CTSA program will be far greater than the number of awards made. The CTSA model is about spurring innovation, integration, inclusion, and dissemination, not just among funded CTSA institutions, but at AHCs across the country. Graduates with new degrees in clinical and translational research will be able to apply their knowledge and introduce new approaches in a variety of public and private sector positions. Transparent evaluations of the CTSAs will identify best practices and processes that other institutions can adapt to strengthen or create their own clinical and translational programs. Through this collective response and national research agenda, we can expect to conduct medical research more effectively, so that we may bring effective results faster to the people who need it.

We have great optimism about these new approaches, but we also know there are lessons to be learned about the best approaches for creating and sustaining the "homes" we are building, for bringing basic and clinical research together, for training and managing interdisciplinary teams, and for addressing tensions concerning the way in which AHCs will make promotion and tenure decisions. We know that IT is critical, but costly and complex – not only for the medical community, but for the health-care sector as a whole.

The key to achieving this vision is the ability to ensure that the rapid and fundamental advances in biomedical and behavioral sciences will be translated into patient-oriented research and then further applied to real-world practice. We recognize that growing barriers between clinical and basic

research, along with ever increasing regulatory and other complexities involved in conducting clinical research, make it more difficult to translate new knowledge to the clinic – and back again to the bench. Disseminating research results and ultimately having them adopted by community health-care providers, patients, and the public also poses unique challenges and requires extensive participation, dialogue, and public trust. As such, these challenges are limiting professional interest in the field and hampering the clinical research enterprise at a time when it should be expanding.

The opportunities have never been greater to use modern research advances in genomics and proteomics and other novel strategies to bring new insights into the study of disease and human populations. We need to take advantage of these opportunities and transform how we practice medicine. By expanding our vision beyond the curative model and intervening earlier in the treatment process, we have the potential to stop diseases before they can occur. The framework for this new vision is centered on four key concepts, or the *4Ps*: *predictive*, *personalized*, *preemptive*, and *participatory* medicine. Practicing medicine in this way will help us move more quickly to understand the fundamental causes of diseases at their earliest molecular stages so that we can reliably *predict* how and when a disease will develop and in whom. Because we now know that individuals respond differently to environmental changes according to their genetic composition and their own behavioral responses, we can envision the ability to precisely target or *personalize* treatments. Ultimately, this individualized approach, completely different than how we treat patients today, will allow us to *preempt* disease before it occurs. In order to realize this vision, we must explore ways to enhance public trust and encourage more active *participation* from our patients and their communities in shaping the future of medicine and improving the health of our nation.

CONFLICT OF INTEREST

The author declared no conflict of interest.

Note to the Editor:
A second Request for Applications for CTSAs has been issued calling for the next round of submissions to be made on 17 January 2007, with awards expected for fall 2007. The Request for Applications is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-002.html. For more information about this initiative that was developed with extensive input from the research community, visit http://www.ncrr.nih.gov/clinicaldiscipline.asp.

1. Zerhouni, E.A. & Alving, B.M. Clinical and Translational Science Awards: a framework for a national research agenda. *Translational Res.* **148,** 4–5 (2006).