

SOUNDING BOARD

## Translational and Clinical Science — Time for a New Vision

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It is the responsibility of those of us involved in today's biomedical research enterprise to translate the remarkable scientific innovations we are witnessing into health gains for the nation. In order to address this imperative, we at the National Institutes of Health (NIH) asked ourselves: What novel approaches can be developed that have the potential to be truly transforming for human health? To help crystallize these ideas and develop tangible strategies to advance our efforts, three years ago the NIH initiated a series of consultations with the research community to define major scientific trends collectively, with the goal of identifying thematic areas that no single NIH institute or group of institutes could tackle alone, but that the whole of the NIH needed to address.

This effort led to the development of the NIH Roadmap for Medical Research,<sup>1</sup> with three fundamental themes. First, we identified the need to stimulate the development of novel approaches to unravel the complexity of biologic systems and their regulation, which we encapsulated in the "New Pathways to Discovery" theme. Second, since progress is often made at the interface of preexisting disciplines, we explored ways to reduce the cultural and administrative barriers that often impede such research. To invoke an era in which scientists can cooperate in new and different ways, we drafted novel programs under the theme of "Research Teams of the Future." One of these innovative programs is the Pioneer Award, in which the NIH provides unprecedented intellectual freedom to highly creative thinkers investigating problems of biomedical and behavioral importance.

Third, we heard resounding concern from basic, translational, and clinical researchers alike that their interactions were becoming more remote and difficult, that clinical research was increasingly less attractive to new investigators, and that clinician-scientists were moving away from patient-oriented research. It was clear that instigating renovations in translational and clinical science was

paramount among the NIH's immediate responsibilities. This led us to formulate the third Roadmap theme, "Re-engineering the Clinical Research Enterprise."

Translational and clinical research are core components of a full-spectrum biomedical research enterprise. Yet, these critical arenas of research are hampered by increases in costs and complexity, a dearth of information systems, and increases in the regulatory burden. An explosion in clinical-service demands and reduced financial margins have sharply cut protected research time for many clinical and translational researchers and diluted the time and attention devoted to the research mission of academic institutions. The inevitable result of these changes has been, for example, difficulties in the recruitment and retention of human subjects in clinical trials and, ultimately, considerable delay in the completion of critical studies.

It is more and more difficult to recruit, mentor, and retain a critical mass of clinical and translational scientists. Proper training and mentoring of scientists capable of conducting truly innovative patient-oriented research require dedicated time away from the escalating pressures of clinical-service demands. At the same time, the increasingly complex resources needed to conduct modern clinical and translational research are either missing or scattered. There has been little investment in methodologic research to improve the tools used by clinical and translational scientists. Bioinformatics, bench-to-bedside laboratories, and statistical cores are not integrated in a manner that promotes, for example, both outstanding research and innovation in study design leading to a more efficient end result.

At no other time has the need for a robust, bidirectional information flow between basic and translational scientists been so necessary. Advances in our understanding of biologic systems and the development of powerful new tools that can be applied at both the bench and the bedside —

genomics, proteomics, transgenic animal models, structural biology, biochemistry, and imaging technologies — offer unprecedented prospects for advancing knowledge of human disorders in a translational context. Moreover, it has also become clear that available animal models of human disease are often inadequate, necessitating even more research on human populations and biologic samples.

In an attempt to address these concerns, the NIH has funded facilities, resources, or both to bolster clinical and translational research, such as the General Clinical Research Centers, grants for individual or institutional training and mentoring, support for disease-specific centers, clinical-trial networks, biospecimen repositories, molecular-screening libraries, and more recently, loan-repayment programs designed to attract and retain scientists to this field. Currently, the NIH spends about 36 percent of its budget on clinical research and training activities. Yet, the concerns persist, and more must be done.

Today, there is good reason to believe that the scope of knowledge and expertise needed to be an effective translational or clinical scientist can no longer be acquired “on the job,” as was done in the past. Although we have made every effort to provide the support functions for translational and clinical research, there is a call for training in a wider range of skill sets that span the biomedical and behavioral sciences and make use of far more advanced and more complex resources and methods than ever before. We may have failed to recognize that clinical and translational science is an emerging discipline that encompasses both the acquisition of new knowledge about health and disease prevention, preemption, and treatment and the methodologic research necessary to develop or improve research tools. Clinical and translational researchers require more dedicated and structured learning time and a clear path for both promotion and tenure, combined with opportunities for true scientific inquiry in an intellectual environment conducive to such endeavors.

We now aim to stimulate the development of a brighter vision for translational and clinical research, to ensure that these disciplines remain powerful engines of creativity. We offer the opportunity for change to those who share a vision and commitment to innovation and experimentation. As the world’s largest public funding agent for clinical research, the NIH has the responsibility to work toward dissolving the artificial barriers that

inevitably spring up in any large organization. We persevere in our determination to provide opportunities for the research community and to challenge the status quo in transformative ways, through a “bottom-up” consultative approach. Already, many institutions are offering innovations within their own environments — creating integrative academic structures that include new doctoral-degree programs that have been explicitly designed to grapple with the complex challenges posed by the clinical and translational science of the 21st century.

Drawing from the experience of the Roadmap and the extensive community input, the NIH is announcing a request for applications to launch a new program that will fund institutional Clinical and Translational Science Awards (CTSAs). Through this mechanism (<http://grants.nih.gov/grants/guide/notice-files/NOT-RM-05-013.html>), applicants may propose transformative efforts appropriate to their own institutions. The CTSAs will advance the assembly of institutional academic “homes” that can provide integrated intellectual and physical resources for the conduct of original clinical and translational science. We anticipate that the creative installation and development of these environments will, over time, enhance the theoretical underpinnings of the discipline, provide much-needed educational programs, contribute to the growth of well-structured and well-recognized career pathways, and provide a research environment that is more nimble, conducive to, and responsive to the demands of modern translational and clinical research.

The NIH wishes to provide flexibility and support to institutions who choose to “re-engineer” their own clinical and translational research programs in order to combine a number of existing NIH-funded programs creatively. To allow institutions to build an innovative and integrated program, the NIH is asking applicants to consolidate General Clinical Research Centers, T32 and K12 programs, and other resources, as appropriate. These resources may be augmented by substantial NIH Roadmap funding that has been redirected from other initiatives and targeted to the CTSA program, with the National Center for Research Resources as the lead NIH entity. In addition, as disease burden has shifted from acute conditions to chronic conditions primarily seen in community rather than tertiary centers, new approaches for forging relationships with local and regional community partners will become increasingly critical.

Therefore, opportunities for appropriate partnerships with other institutions and industry will also be encouraged.

The NIH welcomes a multiplicity of tactics, since it is clear that no one model can be successful in all institutional environments. Clearly, the scope of translational and clinical research is so large that a differentiated and focused strategy crafted to the strengths of an applicant's institution and partners is welcome. Institutions that are not ready to apply for a CTSA may apply for a planning grant to give them time to devise such a self-described integrated program. The CTSA program represents the first step in this process. The NIH hopes to lead, listen to, and assist institutions and investigators in transforming themselves over time to meet and exceed the demands of the modern age, as we strive to remain — collectively — the best clinical research enterprise in the world.

Underlying these efforts is our belief that in addition to the much-needed improvements in the policies and practices of health care delivery as we know it today, medical and public health practices

in this nation will have to undergo a profound transformation in the coming decades if we are to succeed in providing access to care for all Americans at reasonable costs. Given that knowledge of many fundamental aspects of biology in health and disease is still insufficient to translate current findings reliably into new and more effective prevention and treatment, this goal can be attained only through continuous investment and advances in basic biomedical and behavioral discovery coupled with efficient translational science. It is our intention and hope that this focused and significant commitment to the creation of a new, vital, and reinforced academic discipline and home for translational and clinical science — along with an explicit effort to maximize the effectiveness of NIH resources directed to this area of research — will ensure that extraordinary scientific advances of the past decade will be rapidly captured, translated, and disseminated for the benefit of all Americans.

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1. Zerhouni E. The NIH Roadmap. *Science* 2003;302:63-72.

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