# Translational Research Working Group Roundtable I
# February 23-24, 2006
# Executive Summary

*To the individual who devotes his life to science, nothing can give more happiness than when the results immediately find practical application. There are not two sciences. There is science and the application of science, and these two are linked as the fruit is to the tree. –Louis Pasteur*

## *Introduction*

On February 23 and 24, 2006, the National Cancer Institute (NCI) sponsored the first of two planned Translational Research Working Group (TRWG) Roundtables with the goal of obtaining substantive, multidisciplinary advice from invited participants on the issues in translational research that are most relevant to NCI's mission. During her opening remarks, Dr. Anna Barker, NCI's Deputy Director for Advanced Technologies and Strategic Partnerships, noted, "We stand at an inflection point in the conquest of cancer, with an unprecedented level of understanding and unimagined possibilities for progress." In the past century, medical systems were established to treat existing disease; morphologic and pathologic diagnosis has driven treatment. This approach is expensive and not sustainable in the 21st century, due the increasing complexity of infrastructure systems and of the understanding of cancer itself. There will need to be a shift toward targeted interventions for cancer prevention, prediction, and personalization of medical care—a shift that demands a "revolution" in the field of medical research to streamline the path from discovery to clinical implementation. For example, developing good biomarkers, as well as the means to prioritize, validate, and utilize them, will be crucial. Translational research will require multidisciplinary collaboration, coordination of complex infrastructures, and streamlining of procedures to maximize efficiency. Toward this end, NCI has embarked on an effort to evaluate its current direction in translational research, convening the TRWG to spearhead the process.

## *Charge of the TRWG and Purpose of the Roundtable*

NCI currently operates a rich "bench to bedside and back" research infrastructure, including clinical center grants, consortia, the Early Detection Research Network (EDRN), P01s, Specialized Programs of Research Excellence (SPOREs), R01s, etc. Nonetheless, advances in cancer biology, the evolving scientific landscape, and changing demographics, offer enormous opportunities for accelerating progress and improving public education and clinical practice. NCI has charged the TRWG with evaluating NCI's current investments in translational research and envisioning its future—both short-term adjustments and long-term improvements—in an inclusive, representative, and transparent manner.

During this first Roundtable, the TRWG sought advice, guidance, and recommendations from invited experts to assist the working group in developing its final recommendations to the NCI. Participants were also asked to envision an optimal translational research program—its organization (e.g., investigator-initiated versus facilitated research), orientation (e.g., disease-based versus pathway based), and management. A secondary

purpose of the first TRWG Roundtable was to effectively communicate the TRWG's purpose, goals, and processes to the broader research and cancer advocacy community. While the translational research continuum spans from basic scientific discovery to dissemination and widespread adoption, a number of efforts, including the Clinical Trials Working Group (CTWG), have recently explored the clinical aspects of translation; thus, the TRWG will focus its efforts on early translation (i.e., partnerships and collaboration, intervention development, and Phase I and II clinical trials).

The TRWG has sought and will continue to seek public comment on key questions through its Web site, http://trwg.cancer.gov. The Working Group is also engaged in an effort to evaluate the breadth and depth of NCI's current translational research portfolio in order to inform the TRWG's work. Concurrently, the TRWG is conducting a process analysis of current translational research processes to identify bottlenecks in translational processes; describe the roles of NCI, industry, and academia in various processes; and discover lessons learned and gaps in translational research pathways.

### *Roundtable Participants*

The TRWG cast a wide net, inviting 203 experts from 29 states and the United Kingdom and from many fields and subspecialties to ensure comprehensive representation and maximize innovation. Representatives were invited from academic cancer centers; the biomedical and pharmaceutical industries; the patient education and advocacy community; cancer foundations; schools of business, management, law, and public policy; venture capital; as well as Federal agencies, including NCI, the Food and Drug Administration, the Centers for Medicare and Medicaid Services, and the National Institute of Standards and Technology. An effort was also made to invite researchers supported by a variety of programmatic and funding mechanisms, both within and outside of the NCI. Diverse areas of expertise among participants greatly enriched Roundtable discussions and included adult and pediatric oncology; hematology; gastroenterology; radiology and imaging; biochemical sciences; molecular biology; immunology; biomedical engineering; biostatistics and applied mathematics; bioinformatics and information technology; cancer prevention; behavioral sciences; developmental therapeutics; obstetrics and gynecology; survivorship and patient advocacy; pharmacology; intellectual property, commercialization, and technology transfer; bioethics; training; research and clinical trials; nursing; regulatory affairs; insurance and reimbursement; pathology; urology; genetics; and communications. Many working groups, advisory boards, and task forces that have grappled with issues in translational science were represented. Roundtable discussions were fruitful, and resulting recommendations will be central to the TRWG's deliberations, decisions, and activities.

### *Discussion Framework: Three Perspectives on Translational Science*

#### Developmental Pathways

During its December 2005 meeting and subsequent months, the TRWG devised five "developmental pathways" to describe the path that different kinds of basic discoveries take from the point of concept to realization of a stated clinical goal:

- Agent Developmental Pathway
  - *Clinical Goal:* Develop an agent (drug or biologic) for therapy or prevention that interacts with a molecular or cellular target and reduces cancer development or progression.
- Risk Assessment Device Pathway
  - *Clinical Goal:* Develop a molecular analysis or imaging assay for screening, diagnosis, prognosis, or prediction that correlates with cancer outcome or risk and requires development of a protocol, reagents, and/or instrumentation.
- Immune Response Modifier Pathway
  - *Clinical Goal:* Develop a small molecule, peptide, protein, or cell-based vaccine or a general immune modifier that induces an antitumor cell response and requires development of an antigen, a delivery vehicle and/or an immune modulator, such as an adjuvant, cytokine, chemokine, etc.
- Interventive Device Pathway
  - *Clinical Goal:* Develop a device for improved surgical, radiation, or other interventive treatment.
- Lifestyle Intervention Pathway
  - *Clinical Goal:* Demonstrate a behavioral or exposure change (e.g., tobacco use, nutrition, physical activity, obesity, toxic chemical exposure) that reduces cancer development or progression.

These pathways served as a framework and guide for Roundtable discussions and were woven throughout the meeting as points of reference. During the first breakout sessions, participants reviewed case studies related to each pathway; discussed associated resources, prioritization of translational research opportunities, coordination, communication, evaluation metrics and milestones, and barriers; and proposed recommendations for improving each of these areas in relation to each developmental pathway.

## Crosscutting Themes

The TRWG has identified a number of crosscutting themes that have significant impact on the effectiveness and success of translational research efforts. During the second breakout sessions, Roundtable participants discussed the following crosscutting issues and made short- and long-term recommendations to improve current practices and facilitate translational research.

**NCI process for identifying and soliciting opportunities in translational research.** The group discussed ways in which NCI could facilitate identification of the most important opportunities in translational research and considered whether a process should be developed to prioritize such opportunities for the purposes of developing targeted NCI solicitations and communicating priorities to the academic community. The group also debated optimal ways of organizing such a prioritization system and stakeholders that should be involved in the process.

**Funding.** Noting that roughly 35 percent of NCI's FY2004 budget (including intramural and extramural programs) was devoted to research that reasonably could be categorized as "translational," the group debated whether this significant amount of money is being

invested most effectively and considered the highest priority areas for NCI translational research investment.

**NCI review process for translational research.** During this session, participants discussed whether NCI should designate separate funds for translational research and whether the review process should include specific criteria or guidelines to be used in evaluation and scoring of translational research grant applications. The group also considered how to best manage the overlap in translational research between basic and clinical research; whether funding mechanisms should be developed to enable institutes with strong translational programs, but without great depth, to be competitive; and whether part of the review process should encourage collaboration and/or consortium development.

**Evaluation processes and metrics for translational research.** Participants in this session discussed the unique needs for evaluation metrics in translational research. The group also noted unique challenges in translational research evaluation; for example, metrics may provide a snapshot of activities, but miss some activities in the pipeline. In addition, less than 10 percent of phase I drugs/studies go forward to phase II or beyond. Thus, there is a need for positive, tangible measurements from an early phase clinical trials to guide future research.

**Coordination, collaboration, and communication.** The group debated whether translational research would be more effective by relying on the ideas arising from individual investigators or by using facilitated mechanisms transcending individual investigators. The group also discussed the ideal organizational premise for translational research and the policies, procedures, and structures within NCI, academic medical centers, and industry that currently exist or could be developed or improved to facilitate the coordination, collaboration, and communication that are essential to translational research.

**Management approaches.** During this session, participants discussed whether a more active form of management in NCI-funded translational research is needed and proposed different management approaches for translational research, including academic versus industry models.

**Facilities and technologies.** Participants discussed the availability, accessibility, and duplication of facilities and technologies for translational research, as well as inventory and coordination of current and future infrastructure and core services. Core services identified as necessary for translational research included medicinal chemistry, pharmacokinetics/pharmacodynamics, experimental pathology/toxicology, clinical trials regulatory affairs, GMP/GLP, small molecules, genes, vaccines, biologics, cells, radiopharmaceuticals, and advanced engineering and device development.

**Availability, integration, and training of a translational science workforce.** This session explored unique requirements of a translational research workforce and proposed ways of training such a workforce (i.e., cross-training versus translational specialty training), providing incentives for talented scientists to enter translational research, and integrating translational researchers with their basic and clinical colleagues.

**Commercialization.** Participants in this session discussed means of facilitating commercialization of promising discoveries. Specifically, the group proposed solutions for improving early-stage communication among NCI, industry, and academia; enhancing integration of industry into NCI-funded translational research efforts; addressing intellectual property and licensing issues; enhancing access to legal, regulatory, manufacturing, and quality control skills; and improving communication with the U.S. Food and Drug Administration (FDA).

### Populations Served

Six distinct populations that are important beneficiaries of translational science were identified, and the third series of breakout sessions were devoted to discussing crosscutting themes in translational research from the perspective of these populations and identifying issues that are unique to those patients. The six populations discussed were:

**At-Risk Populations.** Subpopulations of the "at-risk" population include small populations of individuals who are high-risk due to inherited susceptibility, as well as a large population of individuals who are at increased risk relative to the entire population due to lifestyle and high-risk behaviors. The type of intervention largely depends on the risk to benefit ratio.

**Early-Stage Disease.** Early-stage patients are often seen initially by physicians who are not part of the clinical research team. Early-stage clinical trials and biospecimen donation are key.

**Late-Stage Disease.** Late-stage disease patients include those whose cancers are metastatic, and they are often older patients with comorbid conditions. Late-stage disease is the traditional entry point for clinical trials, and a key tension is palliation versus aggressive treatment.

**Pediatrics.** Pediatric oncology research is a unified cooperative group that is able to capture nearly all of the patient population. Unique challenges include the differences in young children versus adults with respect to the tumors themselves, as well as accrual rates to translational trials. A large percentage of the pediatric population is cured; therefore, there are unique survivorship and late-effects issues.

**Rare Cancers.** A rare cancer is one with an incidence of less than 15 cases per 100,000, or a cancer with fewer than 40,000 cases per year in the United States. A key challenge in research of rare cancers is obtaining sufficient cases for well-powered clinical trials.

**Minority and Underserved Populations.** Cancer disparities may be widening. Including minorities and underserved patients in clinical trials is crucial, but there are often comorbidities that restrict eligibility for enrollment.

## *TRWG Future Steps*

Important recommendations and solutions were proposed during the Roundtable, and the TRWG also had the opportunity to examine translational research from the unique perspective of some participants. For example, during the meeting, participants heard from Dr. David Kerr about a promising program, the National Translational Cancer Research Network (NTRAC) recently implemented in the United Kingdom to build

networks of cancer centers to improve cancer care. The TRWG will refine the developmental pathways according to input received from Roundtable participants and will compile and ponder the results of the Roundtable discussions as well as the public comments received via the TRWG Web site in the months to come. Using these recommendations, the TRWG will develop a draft translational research model and synthesis of recommendations, which will be made available for public comment during the Summer of 2006. A second Roundtable will be convened in the Fall of 2006 to discuss the draft translational research model, recommendations, and evaluation results, and to solicit ideas for implementation. Based on these deliberations, the TRWG will develop an implementation plan, a finalized translational research model, and recommendations for presentation to the National Cancer Advisory Board in February, 2007. This first TRWG Roundtable represents an important step in the process—capturing input and ideas from the broader research community regarding NCI's role and activities in translational research.