# Translational Research Working Group
# Public Roundtable II
# Executive Summary

## Background

In the fall of 2005, the National Cancer Institute (NCI) convened the Translational Research Working Group (TRWG) to evaluate the status of the current NCI investment in translational research and envision its future in an inclusive, representative, and transparent manner. The TRWG comprises 63 individuals representing a diverse array of disease populations, scientific areas, and NCI programs. Since its inception, the TRWG has generated a number of products to assist in its work and solicited input from a variety of external groups. It is now working to develop recommendations and related implementation strategies for near-term adjustments to NCI programs as well as a long-term vision for the NCI translational research enterprise.

## Goals of the Roundtable

On October 16-17, 2006, the TRWG convened the second of two public Roundtables. The 89 invited attendees possessed a broad range of expertise and included representatives from academic medical centers; patient advocacy groups and foundations; professional societies; biotechnology and pharmaceutical companies; and government agencies. The goals of the Roundtable were to: 1) share products generated by the TRWG to date, 2) obtain broad, substantive input regarding draft TRWG initiatives, and 3) solicit recommendations regarding implementation of these initiatives.

## TRWG Products to Date

*Definition of Translational Research.* The TRWG defines translational research as research that transforms scientific discoveries arising in the lab, clinic, or population into new clinical tools and applications that reduce cancer incidence, morbidity, and mortality. The work of the TRWG focuses on early translation, as defined by the President's Cancer Panel in its 2004-2005 annual report.

*Developmental Pathways to Clinical Goals.* The TRWG developed five pathways to clinical goals that represent translational research activities related to the development of agents, risk assessment devices, immune response modifiers, interventive devices, and lifestyle interventions. These diagrams outline the processes through which fundamental scientific discoveries are transformed into clinical applications. Although developed to facilitate the work of the TRWG, the pathways may also serve as tools to monitor progress of and identify gaps in translational research.

*Process Analysis.* The TRWG performed case studies of translational research "successes" in order to gain insight into common elements of success, bottlenecks, and the roles of academia, industry, and NCI in translational research. Twenty case studies spanning the five developmental pathways to clinical goals were completed; the analysis revealed notable diversity in the mechanisms and research teams that contribute to progress in translational research.

*Portfolio Analysis.* The TRWG analyzed the NCI fiscal year 2004 research portfolio to generate a better understanding of NCI's overall effort in translational research. The exercise indicated that translational research is funded by most NCI Divisions, Offices, and Centers through a range of mechanisms, including individual, collaborative, and facilitated awards. However, the effort also revealed that the current coding system does not allow for meaningful, detailed quantitative assessments of the translational content of grants.

## External Input

The TRWG has solicited public input on several occasions throughout the course of its work. The first public Roundtable in February 2006 brought together experts from many areas of the cancer community to consider translational research from three different perspectives – developmental pathways to clinical goals, crosscutting themes, and populations. The 375 recommendations that emerged from this Roundtable in combination with the input received through the TRWG Web-based public comment platform established the foundation for future work of the TRWG and heavily influenced the subsequent development of draft initiatives and implementation concepts. The input gathered at the current Roundtable regarding the draft initiatives and implementation concepts will be supplemented with comments obtained through a second Web-based public comment session. Comments will also be received from other interested communities, including the American Society of Clinical Oncology Translational Research Task Force, the Specialized Programs of Research Excellence (SPORE) Directors, the Cancer Center Directors, and NCI staff.

## TRWG Draft Initiatives

Assessment of the current NCI investment in translational research in combination with public comment received by the TRWG revealed a number of existing obstacles to translational research. To address these obstacles, the TRWG formed six subcommittees: Organization and Funding; Core Services Coordination; Prioritization; Project Management; Training and Workforce; and External Integration. Working in subcommittees and as an integrated group, the TRWG developed a series of draft initiatives and related implementation concepts. These 17 initiatives were grouped into three themes: Coordinated Management, Tailored Funding Mechanisms, and Operational Effectiveness. These themes formed the basis of three breakout sessions during which Roundtable participants discussed the initiatives and potential options for their implementation.

### *Coordinated Management Draft Initiatives*

Roundtable participants were grouped by interest and expertise into one of eight breakout groups. Although the primary goal of the session was to discuss the overall value of the Coordinated Management initiatives (A1-A4), each group was also charged with considering the initiatives and implementation concepts from the perspective of one of the following populations or pathways to clinical goals.

- Agents (Therapy)
- Agents (Prevention)
- Immune Response Modifiers (Therapy/Prevention)
- Risk Assessment Devices (Imaging) and Interventive Devices
- Risk Assessment Devices (Molecular Markers)
- Lifestyle Alterations
- Pediatric and Rare Cancers
- Minority and Underserved Populations

Following the breakout sessions, the session chairs participated in a moderated panel discussion to report session results to the larger group.

#### Draft Initiative A1: Establish a flexible, integrated organizational approach that coordinates early translational research opportunities across NCI.

Overall support for the concept of establishing a flexible, integrated organizational approach to coordinate translational research opportunities across NCI was expressed; however, participants

cautioned against the creation of unnecessary bureaucracy. The need for interaction between different components of translational research was emphasized. The pros and cons of coordinating translational research by organ and/or pathways to clinical goals were discussed.

### Draft Initiative A2: Designate a specific portion of the NCI budget for early translational research.

There was a wide range of responses to the proposal that a specific portion of the NCI budget be designated for translational research. Several groups expressed support for the concept, but were unable to identify the appropriate portion of the budget that should be designated; in general, these groups felt that translational research should at least maintain the current level of funding. Other groups were unsupportive of the initiative, stating that budget allocations should be based on evaluation of need and/or record of success.

### Draft Initiative A3: Establish a coding and tracking system that accurately captures the nature and scope of the NCI early translational research enterprise.

All of the breakout groups supported the establishment of an improved coding and tracking system. It was suggested that the developmental pathways to clinical goals would be useful in the creation of a new system. The coding/tracking system should also incorporate metrics to facilitate evaluation of progress in translational research.

### Draft Initiative A4: Establish a distinctive prioritization process for early translational research to identify and prioritize research goals and opportunities and select specific projects to realize these goals.

Most of the breakout groups expressed support for the establishment of a prioritization process for translational research, although endorsement for the concept was not unanimous. Some of the participants opposed any system of "top-down" research while others supported the concept as long as it is not designed to dictate research activities across NCI. Multiple groups emphasized that the prioritization committee will need to be given sufficient power to carry out the prioritization process. The prioritization process should be largely driven by the extramural community; however, NCI representatives should also be involved.

## *Tailored Funding Mechanism Draft Initiatives*

Roundtable participants were grouped by interest and expertise into one of eight breakout groups. Although the primary goal of the session was to discuss the overall value of the Tailored Funding Mechanism initiatives (B1-B5), each group was also charged with considering the initiatives and implementation concepts from the perspective of one of the following populations or pathways to clinical goals.

- Agents (Therapy)
- Agents (Prevention)
- Immune Response Modifiers (Therapy/Prevention)
- Risk Assessment Devices (Imaging) and Interventive Devices
- Risk Assessment Devices (Molecular Markers)
- Lifestyle Alterations
- Pediatric and Rare Cancers
- Minority and Underserved Populations

Following the breakout sessions, the session chairs participated in a moderated panel discussion to report the results of their sessions to the larger group.

### Draft Initiative B1: Modify multiproject/collaborative award guidelines and review criteria, as appropriate, to facilitate early translational research.

All of the breakout groups expressed support for modifying guidelines and review criteria to facilitate early translational research. Guidelines and review criteria should encourage collaboration across institutions and programs (e.g., Cancer Centers, SPOREs) and with industry partners. Importantly, funding should be required for any added requirements. In addition to modifying review criteria, there is a need for improved representation of translational research expertise on study sections. It was also emphasized that translational research funding mechanisms must accommodate all five of the developmental pathways to clinical goals.

### Draft Initiative B2: Work with NIH toward developing new R-series and P-series mechanisms tailored toward translational research.

The concept of working with NIH to develop new R- and P-series mechanisms was not rejected, but most of the groups felt that improving the quality of review for translational research is more important. Overall, there is a perception that translational research expertise is lacking on many or most NIH study sections. It was suggested that NCI and the translational research community be more proactive in suggesting potential reviewers for NIH study sections. Another idea was to alter NIH criteria of "significance" and "innovation" to better accommodate translational research projects.

### Draft Initiative B3: Establish a new special translational research funding mechanism to advance prioritized early translational research opportunities rapidly and efficiently.

There was enthusiasm for the concept of establishing a funding mechanism to advance prioritized early translational research opportunities; however, there was a range of ideas regarding the best way to implement such a mechanism, and several potential concerns were raised. Because overcoming barriers is often more important than funding, facilitation was viewed as critical to accomplishing the goals of the mechanism. The use of milestones was viewed favorably, with one group strongly supporting the idea that funds be directly tied to milestone completion. To be effective, the mechanism should be associated with an expedited timeframe for submission, review, and funding.

### Draft Initiative B4: Establish a new funding mechanism for early translational research that requires academic/industry collaboration involving resource sharing and/or cofunding.

The benefit of forging translational research collaborations with industry was recognized; however, there was disagreement about whether these partnerships should be required or only encouraged. Two session chairs reported that the majority of the participants in their groups favored encouraging industry collaboration by building incentives into existing funding mechanisms rather than creating a new mechanism requiring interaction with industry. Similarly, another group stated that addressing the many barriers to academic-industry collaboration should be of primary importance. Several groups felt that mechanisms requiring or encouraging collaboration should not be limited to industry but should include foundations, nonprofit organizations, and other entities.

### Draft Initiative B5: Integrate access to pharmacology, GMP/GLP manufacturing, and/or toxicology services more effectively with milestone-driven early translational research funding mechanisms.

All of the breakout groups supported integration of access to pharmacology, toxicology, and manufacturing services with translational research funding mechanisms. Some thought the effort should be focused on prioritized projects (Draft Initiative B3), while others thought these services should be made more broadly available to all NCI-funded translational researchers. Expediting access to GMP/GLP services by eliminating the need to submit a separate, formal application to these facilities was viewed as critical. Project management was seen as an important part of facilitating the interaction between researchers and GMP/GLP facilities. It was suggested that creation of a database or Web-based resource identifying available resources would be of value to the research community.

## *Operational Effectiveness Draft Initiatives*

Roundtable participants were divided into breakout groups to discuss the eight Operational Effectiveness draft initiatives (C1-C8) and related implementation concepts. Each breakout group focused on a single initiative with the exception of the Workforce and Training group, which considered two closely related initiatives (C7-C8). Following the breakout session, each chair provided a brief overview of the discussion for the larger group.

### Draft Initiative C1: Establish a formal project management structure for early translational research.

The need for project management was widely recognized. Project managers would facilitate identification of and access to resources as well as assist the handoff of projects between different groups. Varying levels of project management training will be required for different participants in the process, including NCI staff and researchers. In order for a project management system to be effectively implemented, NCI staff will need to be committed to the concept and investigators will need to be convinced of its benefit to their research programs. Importantly, project management should be implemented incrementally and evaluated before being expanded into general use.

### Draft Initiative C2: Establish a system to coordinate and promote core services essential for early translational research.

There was support for establishment of a system to coordinate and promote core services for translational research. An analysis should be performed to generate an inventory of existing core service facilities and determine whether perceived redundancies are real; care should be taken to collect meaningful information so the inventory will be useful. A comprehensive database of all NCI-funded core facilities should be established. Each institution should unite all its core services under a single administrative unit; when present, Cancer Centers should fill this role. Review guidelines should be altered to encourage resource sharing, when appropriate, rather than creation of new resources. Also, highly technical core services, such as GMP and proteomics, should be regionalized.

### Draft Initiative C3: Enhance quality and accessibility of annotated biospecimen repositories.

There was support for the concept of enhancing the quality of and accessibility to annotated biospecimen repositories. To this end, NCI should develop a common informed consent template for tissue collection, annotation, and analysis that should apply to both current and future uses of the tissue. NCI should also facilitate concurrence on and dissemination of common elements for standardized specimen collection. NCI should encourage standardized specimen collection in all of

the studies it supports and provide funds for specimen collection and processing as well as for banking and continued annotation. It was recognized that a fair, feasible approach to industry partnerships with regard to biospecimens would need to be carefully developed. Advocacy groups could play a central role in this process, both by providing financial support and brokering specimen collection and distribution.

### Draft Initiative C4: Promote mechanisms for rapid negotiation of intellectual property agreements.

NCI should consider developing IP guidelines for translational research similar to those used by the National Human Genome Research Institute, which encourage nonexclusive licenses and promote the early use of templates. When appropriate, NCI should consider making funding contingent upon completion of IP negotiation. NCI should also consider creating a repository to facilitate investigator access to compounds and other resources. The repository could include compounds developed within the NCI as well as those for which patent protection has expired. NCI could also make an effort to collect and collate compounds from the pharmaceutical industry; investigators and companies would then be responsible for negotiating IP issues.

### Draft Initiative C5: Promote integration of industry in the NCI early translational research enterprise.

NCI should work to include industry in advisory and consultative capacities, but care must be taken to select the representatives with appropriate expertise and interest. It would be beneficial to have NCI, academia, and industry participate in joint summits to identify areas of interest and need. It may also be of value to generate a structured catalogue of needs and interests to facilitate identification of potential areas for collaboration.

### Draft Initiative C6: Enhance interaction and collaboration with foundations and advocacy groups to advance early translational research.

NCI should take advantage of the fact that patient advocates have become increasingly sophisticated and are skilled in communications as well as other areas. Advocates should be engaged early and consistently. Areas in which NCI should work with foundations and advocacy groups include prioritization, education, review, strategy development, and research support. Foundations and advocacy groups can help identify gaps in the activities of NCI and industry. These organizations can sometimes complement NCI's research investment by providing supplemental funds to existing grants. Foundations and advocacy groups are specially poised to help with IP negotiations and regulatory issues. Existing venues for advocate involvement should be optimized and publicized.

### Draft Initiative C7: Expand and enhance training in early translational research across disciplines and stages of professional development.

### Draft Initiative C8: Enhance incentives for pursuing careers in early translational research.

There was consensus regarding the need for training programs focused on core competencies required for early translational research. There is a specific need for training in drug and device development and regulatory sciences. Training in team science and translational research should be mandated, as should protected time for researchers to develop their careers. Currently, translational researchers are often required to perform income-generating activities, which detract from their ability to develop productive research programs. The lower salaries of researchers compared with clinicians also deter investigators from pursing careers in translational research.

### *TRWG Future Steps*

The TRWG will finalize its recommendations over the coming months, taking into account input provided by Roundtable participants as well as that collected through the Web-based public comment forum. The final TRWG report will be presented to the National Cancer Advisory Board in February 2007.