MEETING SUMMARY
PRESIDENT'S CANCEL PANEL
TRANSLATING RESEARCH TO REDUCE THE BURDEN OF CANCER

November 1, 2004
Houston, TX

OVERVIEW

The purpose of the meeting, the third of four regional meetings, was to examine barriers to progress in translating cancer research into reductions in suffering and death due to cancer. The President's Cancer Panel (PCP, the Panel) is seeking input to help develop its recommendations to the President of the United States, the U.S. Congress, the Secretary of Health and Human Services (HHS), and the broader community of researchers, policy makers, advocates, and others.

PARTICIPANTS

President's Cancer Panel

LaSalle D. Leffall, Jr., M.D., F.A.C.S., Chair

Margaret Kripke, Ph.D.

Lance Armstrong

National Cancer Institute

Andrew C. von Eschenbach, M.D., Director, NCI

Maureen O. Wilson, Ph.D., Assistant Director, NCI, and Executive Secretary, PCP

Sarah Birckhead, M.S.W., Special Assistant, Office of the Director, NCI

Heather Kapp, M.S.W., M.P.H., Communications Fellow, PCP

Karen Parker, M.S.W., Special Assistant, PCP

David Pugach, J.D., Legislative Analyst, NCI

Abby Sandler, Ph.D., IRO, NCI

Speakers

J. Carl Barrett, Ph.D., Director, Center for Cancer Research, NCI

Robert C. Bast, Jr., M.D., Vice President, Translational Research, The University of Texas M. D. Anderson Cancer Center

Eric Berger, M.P.A., Vice President of Planning and Public Policy, US Oncology

Kevin T. Brady, M.P.H., Acting Director, Division of Cancer Prevention and Control, Centers for Disease Control and Prevention

Otis W. Brawley, M.D., Associate Director for Cancer Control, Winship Cancer Institute, Emory University

Deborah Collyar, B.S., President, PAIR: Patient Advocates in Research

William Dalton, M.D., Ph.D., CEO/Center Director, H. Lee Moffit Cancer Center and Research Institute

Harry R. Gibbs, M.D., Acting Professor and Vice President for Institutional Diversity, The University of Texas M. D. Anderson Cancer Center

Jack Gill, Ph.D., Founder and General Partner, Vanguard Ventures

Martha Gray, Ph.D., Director, Division of Health Sciences and Technology, Massachusetts Institute of Technology

Elmer Emilio Huerta, M.D., M.P.H., Director, Cancer Preventorium, Washington Cancer Institute, Washington Hospital Center

Anthony Infante, M.D., Ph.D., Professor, The University of Texas Health Sciences Center–San Antonio

William M. Jordan, D.O., President/CEO, Texas Cancer Care–The Center for Cancer and Blood Disorders

Paula Kim, President of Scientific and Government Affairs/Cofounder, Pancreatic Cancer Action Network

Lynn Matrisian, Ph.D., Professor and Chair, Department of Cancer Biology, Vanderbilt University School of Medicine

Thomas Mays, Ph.D., J.D., Counsel for Intellectual Property, Bureau of Competition, Office of Policy and Coordination, Federal Trade Commission

John Mendelsohn, M.D., President, The University of Texas M. D. Anderson Cancer Center

Paul Papagni, J.D., Director, Institutional Review Board, UMDNJ–Robert Wood Johnson Medical School

Amelie G. Ramirez, Dr.P.H., M.P.H., Professor, Department of Medicine, and Member, Executive Committee, The Cancer Center, Baylor College of Medicine

Lynn M. Schuchter, M.D., Associate Professor of Medicine, Abramson Cancer Center, University of Pennsylvania

Jonathan Simons, M.D., Director, Winship Cancer Institute, Emory University

OPENING REMARKS—DR. LaSALLE D. LEFFALL, JR.

On behalf of the PCP, Dr. Leffall welcomed invited participants and the public. He provided a brief overview of the history and purpose of the Panel and the aims of the current series of meetings on translating research into practice. Dr. Leffall explained that the meeting would consist of three panel discussions, each addressing a unique aspect of translating research into reductions in the burden of cancer. Abstracts submitted in advance by the speakers were made available during the meeting.

WELCOME—DR. JOHN MENDELSOHN

Background

Dr. Mendelsohn combines experience in clinical and laboratory research with administrative expertise in order to guide The University of Texas M. D. Anderson Cancer Center in the new century. Since becoming president in July 1996, he has recruited a visionary management team and implemented new priorities for integrated programs in care, research, education, and cancer prevention. Dr. Mendelsohn serves as the Founding Editor of *Clinical Cancer Research*, a bimonthly clinical research journal published by the American Association for Cancer Research. He was Founding Director of the Cancer Center at the University of California, San Diego, and served as Chairman of the Department of Medicine at Memorial Sloan-Kettering Cancer Center for 11 years. For almost three decades, Dr. Mendelsohn has been at the forefront in understanding how growth factors regulate the proliferation of cancer cells by activating surface receptors that control key cell-signaling pathways.

Key Points

- The M. D. Anderson Cancer Center has one of the largest clinical research programs in the nation. In 2003, the Center registered 24,000 new patients and enrolled 12,000 patients in therapeutic clinical trials. The Center, which has almost 900 faculty members focusing on the elimination of the burden of cancer through research, teaching, and patient care, receives more NCI grant support than any other university in the United States.

PANEL DISCUSSION I—BARRIERS TO TRANSLATING RESEARCH INTO REDUCTIONS IN THE BURDEN OF CANCER

INTRODUCTION—DR. JOHN MENDELSOHN

Dr. Mendelsohn introduced the panel members.

MR. ERIC BERGER

Background

Mr. Berger is Vice President of Planning and Public Policy at US Oncology. He is responsible for the Federal and state legislative and regulatory affairs of the network, its public outreach and patient advocacy initiatives, and its strategic planning activities. Beginning in April 1995, Mr. Berger was a member of the professional staff of the Commerce Committee of the U.S. House of Representatives. In that capacity, he was responsible for health policy legislation, including Medicare, Medicaid, FDA, NIH, and health insurance reform. Prior to serving as a congressional staffer, Mr. Berger served as the Legislative and Policy Director for Health and Human Resources in the administration of Virginia Governor George Allen.

Key Points

- US Oncology is a nationwide network of community oncology facilities, physician offices, integrated cancer centers, and similar organizations,. It employs almost 1,000 physicians, including approximately 300 clinical researchers who see 500,000 patients a year and participate in nearly 100 NCI-administered clinical trials. More than 83 percent of all cancer treatment encounters take place in community oncology facilities.
- The Centers for Medicare and Medicaid Services (CMS) will soon release a new regulation that will affect Medicare reimbursement for community oncology. This regulation will clarify the implications of the recently enacted Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA), which significantly reformed the manner in which Medicare provides reimbursement for cancer care services provided in the community setting. The intent of Congress in passing the MMA was to repair a flawed payment system without negatively affecting patient access to care.
- Earlier proposals called for large reductions in spending for community cancer care; after revisions to the legislation, the Congressional Budget Office (CBO) estimated that the final MMA would result in a reduction of only $4.2 billion.
- Analyses of preliminary data provided by CMS suggest that the new regulation will result in a reduction in spending on community cancer care of $5 billion to $7 billion more than the CBO estimate. This would have the kind of negative effect on access to care that the MMA was intended to avoid. The impact of this regulation will not be limited to those covered by Medicare: managed care plans tend to follow the lead of Medicare in setting their reimbursement policies.
- The President's Cancer Panel should closely monitor this new regulation's impact on access to care and participate in the cancer community's dialogue with CMS to ensure that payment system reform and protection of access to community cancer care receive equal emphasis. The new regulation is subject to revision, and the new payment system will not take effect until January 1, 2005.

Discussion: Mr. Berger—Key Points

- In response to passage of the MMA, an alliance of more than 50 organizations involved in community cancer care created a "global access project" to collect data on the impact of changes in the Medicare system. This effort has shown that Medicare beneficiaries without secondary or supplemental insurance who are unable to pay their portion of their health care costs will become an increasing burden upon the hospital delivery system.

MS. DEBORAH COLLYAR

Background

Ms. Collyar, a two-time breast cancer survivor, has been a leader in cancer patient advocacy since 1991. She has paved the way for patient advocate involvement in research for all cancers by applying her considerable business skills and experience, which she developed working in the computer industry. In 1996, she founded a national network of approximately 200 cancer patient advocates called PAIR: Patient Advocates In Research. Recently, Ms. Collyar became the Co-Principal Investigator/Program Director of an NCI-funded Specialized Program of Research Excellence (SPORE): the Patient Advocate/Research Team (PART) program. The PART program helps 56 SPOREs develop local PART teams and helps them surmount major research barriers that thwart the translation of scientific discoveries into care for people with cancer (or those who seek cancer prevention).

Key Points

- The cancer research community is rightfully proud of its many accomplishments, but researchers should not interpret isolated success stories as evidence that the system is moving in the right direction. Most research accomplishments have resulted from individual efforts within a disjointed system that rewards competition rather than cooperation.
- Through events like the recent withdrawal of Vioxx, the public is beginning to understand that the drug development system is broken. The public's perception that the cancer community does not learn from its mistakes leads to a lack of trust in scientists and their research findings.
- Researchers are often reluctant to call attention to problems because they are afraid their careers will be jeopardized. Practical solutions to operational issues are more likely to be found through interaction among all stakeholders, including the advocacy community.
- Building a cancer research system that supports translational research will require substantial, simultaneous changes. The President's Cancer Panel should consider inviting key decision makers to a retreat to develop measurable action steps and a timeline for overhauling the system in strategic areas.
- Reaching the NCI Director's Challenge Goal for 2015 will require a more detailed roadmap than currently exists. Areas that will need increased emphasis include rewards for participating in team science, cross-disciplinary training, and training in communication skills and team leadership. Cancer Centers must be motivated to place greater emphasis on the creation of information networks and implementation of cancer Bioinformatics Grid (caBIG) initiatives.
- The Panel should ask for an accounting of responses to its recommendations.

Discussion: Ms. Collyar—Key Points

- To reward change that produces results, the cancer community must have not only a vision, but also specific, measurable objectives and goals related to that vision. For example, Cooperative Groups should be expected to consolidate operations within a specific timeframe. Each Branch within NCI should have specific objectives related to the overall goal of meeting the 2015 Challenge.
- The NCI culture of management has traditionally been based on a hierarchical, regulatory model. The Institute should look to the business community for models based on distribution of power and facilitation of productivity.
- Since there is no one person directing all Federal efforts against cancer, it would be difficult to convene a retreat of key decision makers representing all stakeholders. This might be feasible if an HHS Departmental mandate required all agencies involved in cancer research and services to participate in a joint cancer translational research initiative.
- Outcomes assessments are rarely conducted because most projects do not plan or budget for them. Institutions conducting clinical trials should be required to develop accrual plans to ensure that a variety of populations and communities are involved, as well as dissemination plans to ensure that findings are communicated.
- Because they are not involved in the business of research, advocacy organizations can play a major role in bringing other stakeholders together to bring the benefits of research to patients in a timely fashion.

DR. WILLIAM DALTON

Background

Dr. Dalton's research interests include biochemical mechanisms of drug resistance and new drug discovery. He is also an expert in the biology and treatment of multiple myeloma. Dr. Dalton was the Founding Director of the Bone Marrow Transplant program at the University of Arizona. From 1997 to 2001, he was Deputy Director of the H. Lee Moffitt Cancer Center and Chairman of the Department of Interdisciplinary Oncology at the University of South Florida. He served as Dean of the College of Medicine at the University of Arizona in Tucson from 2001 to 2002. Dr. Dalton returned to the Moffitt Cancer Center and Research Institute in August 2002 to serve as its Chief Executive Officer and Center Director.

Key Points

- When discussing the continuum of discovery, development, and delivery, it must be remembered that delivery is more than just disseminating information; it is a science unto itself. The delivery enterprise must be a dynamic, real-time system that not only provides information, but also carries information back from the community to inform further discovery and development efforts.
- Communities must be involved from the beginning in the design of trials investigating the application of molecular signatures in cancer screening, diagnosis, and treatment. Early community participation in this process will make it easier to determine whether the use of molecular signatures will have a significant impact on the delivery of interventions.
- Creation of an Internet-based information system will enable real-time linking of patient points of contact throughout the health care research and delivery system. To avoid violating Health Insurance Portability and Accountability Act (HIPAA) regulations, providers will have to ask patients for their consent to follow them over time using shared information. This will create a large database of evidence to determine as efficiently as possible whether new interventions are effective.
- The Moffit Cancer Center in Tampa, Florida, has initiated a 5-year pilot project called Moffit Total Cancer Care. This project involves a network of 15 affiliates that serve almost 20 percent of all cancer patients in Florida. An information system is being developed to coordinate investigator-initiated studies conducted by these affiliates, including trials of molecularly targeted therapies. Patients are being asked for permission to follow them throughout their cancer journeys, including submission of tissues to a central repository and database at the Moffitt Cancer Center.

Discussion: Dr. Dalton—Key Points

- The cancer research community has made some progress in creating interdisciplinary teams and fostering a cross-cultural scientific environment. However, little has been done to involve business specialists in the research enterprise and create an entrepreneurial culture in academia. To take advantage of translational research opportunities, the research culture needs to add a mission-oriented element to its traditional focus on knowledge for its own sake.
- The traditional reward system in academia is based on individual accomplishments, such as grants awarded and papers published. Academic Deans must be persuaded to provide rewards for team participation and contributions to the achievement of mission-oriented goals.
- The affiliates involved in Moffit Total Cancer Care are developing protocols for studies addressed by the pilot project. Every 6 months, the affiliates' principal investigators, along

with representatives of the many physician practices and medical centers involved in the pilot project, meet to discuss the design and implementation of active and proposed protocols.

DR. MARTHA GRAY

Background

Dr. Gray is Director of the Harvard-Massachusetts Institute of Technology (MIT) Division of Health Sciences and Technology (HST) and the Edward Hood Taplin Professor of Medical and Electrical Engineering,. Her research interests center on ways to diagnose and treat cartilage degeneration (arthritis) and include connective tissue physiology, imaging, and microfabrication. She holds key leadership roles in a number of educational projects, including HST's Biomedical Engineering Internship Program, the National Science Foundation's (NSF) Engineering Research Center for Bioengineering Educational Technologies (VaNTH), and Realistic Patient Simulation for Training in Critical Care and Emergency Medicine.

Key Points

- As a metaphor for the challenges intrinsic to translating research accomplishments to advance human health, Dr. Gray quoted cell biologist Ursula Goodenough: "Life can be explained by nothing but its underlying chemistry, just as chemistry can be explained by nothing but its underlying physics, but the life that emerges … is something more than the collection of molecules. Once these molecules came to reside inside cells, they began to interact with one another to generate new processes like motility and metabolism and perception, processes that are unique to living creatures." The "cells" in the development chain from discovery to delivery are diverse, multidisciplinary groups of people. Translational science is accomplished when these groups interact as equals.
- Translational advances are slowed by the dominance of traditionally distinct and nonoverlapping scientific communities that focus on different parts of the process. Changing the scientific and industrial culture would increase the rate of translation. This culture undervalues factors that advance the translational process. Research is disproportionately devoted to basic science.
- There is a vast imbalance between the number of individuals involved in basic research and the number involved in its translation. Much effort has been made to increase the number of M.D.s involved in clinical research, but not enough is being done to encourage Ph.D.s to become involved in addressing unmet medical needs.
- One solution to these problems is establishing a deep and genuine integration of technology and science within each step of the translational process, as well as across the continuum. The research community needs to nurture individuals who are capable of working across disciplinary boundaries to drive this integration.
- HST provides a useful model for integration of engineering and physical sciences with the biological sciences. HST trains physicians, basic scientists, engineers, entrepreneurs, and business leaders. Students and faculty are forced to confront the perspectives of professional and patient communities throughout the translational process. The success of HST graduates over the past 30 years stands as a refutation of the claim that HST has sacrificed depth for breadth.

Discussion: Dr. Gray—Key Points

- The editorial policies of peer-reviewed biomedical research journals contribute to the culture that separates science into nonoverlapping disciplines. Individuals who engage in and support

multidisciplinary research should work together to develop new models for research publications that make translational science more visible.

- Accomplishing a cultural shift in biomedical rsearch will require new educational approaches that expose students to both basic science and patient care. A gradual change should occur as more people with a translational perspective assume positions as Deans and Department Chairs within academic institutions. Federal agencies like NIH can further this cause by supporting broad-based, multidisciplinary research programs. However, efforts should not be limited to students; established investigators can still be trained in new ways of doing things.
- The Panel's recommendations on these issues should be disseminated to leaders of academic institutions. Any ideas that may affect the way the Government allocates resources will be of great interest to that audience.
- The technological advances most likely to produce significant benefits for translational science are bioinformatics and imaging, which are both multidisciplinary areas. They both require deep understanding of both basic science and patient care.

DR. THOMAS MAYS

Background

As Counsel for Intellectual Property in the Federal Trade Commission's Bureau of Competition, Dr. Mays advises on and assists with non-public investigations of mergers and anticompetitive activities. He also assists with litigation involving the Commission that deals with intellectual property issues and comments and advises on draft legislation, policy statements, and reports relating to intellectual property. He has written and spoken on issues relating to intellectual property, technology transfer, and pharmaceutical product development. He is admitted to practice law in the District of Columbia and the states of Maryland and Washington as well as before the U.S. Supreme Court, U.S. Court of Appeals for the Federal Circuit, and the U.S. Patent & Trademark Office.

Key Points

- Dr. Mays began by noting that his comments did not necessarily reflect the views of the Federal Trade Commission.
- The President's Cancer Panel should ask NCI to convene a small working panel of representatives of the research, commercial, and patent law communities to consider and prepare proposals for experimental research exceptions for patent infringement that will promote cancer research while continuing to permit patent owners to protect their commercial interests.
- The United States, unlike Europe and Japan, does not have a statutory research exemption for patent infringement. There has been commentary in the trade press suggesting that pharmaceutical and biotechnology companies should conduct research outside the United States, which would reduce the ability of the United States to compete.
- There have been numerous anecdotal reports of instances in which patents have interfered with research. A report from the Australian Law Reform Commission states that most researchers in Australia are simply ignoring patents, believing that they are exempt; the same thing is happening in this country.
- The National Research Council, which recently issued a report entitled *A Patent System for the 21st Century*, has indicated that the number of letters requesting that a university specifically consider taking a license or cease infringement activities increased between 2002 and 2003.

- Several years ago, a suit was brought against NCI for using a DNA polymerase enzyme; 30 universities became involved in the suit before NCI was able to negotiate a settlement.
- A number of specific exemptions have been proposed. One, which has been promoted by the American Intellectual Property Law Association, addresses use of a patent to learn more about the claimed research findings, but not to use the invention as it was meant to be used in its market.

Discussion: Dr. Mays—Key Points

- There are other legal issues that impinge on translational research, including delays in the initiation of new clinical trials. In the negotiation of clinical trial agreements, each party tends to focus on its own interests. The Association of American Medical Colleges (AAMC) has produced a pamphlet that addresses a number of issues relevant to this problem, including indemnification and intellectual property. The development of model agreements would enable more efficient negotiations.
- A survey of major U.S. universities is currently being conducted by the AAMC in collaboration with several other groups to determine the extent to which investigators feel that patents infringe upon their ability to conduct research.

MR. PAUL PAPAGNI

Background

Mr. Papagni served as Chief Operating Officer of a for-profit post-acute-care venture at the Cleveland Clinic Foundation prior to moving into the areas of research compliance and institutional review board (IRB) concerns. This included development and implementation of internal audit operations and Federal audit management procedures accomplished through coordination and relationship building in a multi-campus structure. As Administrative Director at the UMDNJ–Robert Wood Johnson Medical School and Columbia University/New York Presbyterian Hospital, and as Executive Director for the IRB for the Cleveland Clinic Healthcare System, Mr. Papagni was responsible for operational reorganization; new system design; audit; regulatory compliance; system validation; HIPAA, Good Clinical Practice, and Research Billing Compliance; and budgetary oversight responsibility for IRBs serving multiple campuses.

Key Points

- When issues related to clinical trials are discussed, participants usually include IRB members and investigators, but patients are seldom represented. Patients are a critical part of the translational research process; while researchers bring their expertise to the table, patients bring their lives. Improving patient education will result in increased participation in clinical studies and improved compliance with protocols.
- IRBs in the past have been blamed for slowing the research process. However, when investigators plan ahead and address potential ethical and regulatory issues, problems can be solved before the research plan is presented to an IRB.
- There is a move towards accreditation of IRBs. One major benefit would be consistency in the review of studies involving human subjects and human subject protection programs. Any accredited institution would be able to accept the review of another accredited institution, which would reduce delay in implementing multicenter studies.
- HIPAA is not as complicated as many people believe it is. There are ways to determine the minimum amount of information necessary to get a trial done, build in needed protections, and get authorization from individuals involved. This will expedite the creation of large databases that will benefit future research.

- The Government should support development of "adverse event" databases on a national level so that academic institutions, researchers, and patients can see what types of adverse events are occurring in real time. Cooperation from industry, the Food and Drug Administration (FDA), and the Office for Human Research Protections (OHRP) would be necessary to make these data available.
- To make collaborations viable, it will be necessary break down some of the competition that occurs between institutions and between investigators. Many states have laws that hinder interstate collaborative research.
- The Cancer Institute of New Jersey is establishing a statewide oncology group in which disciplinary sections are developing their own protocols and making them available to their statewide affiliates. This model includes a centralized IRB. The group is also reaching out to industry to streamline the process of establishing clinical trial agreements.

Discussion: Mr. Papagni—Key Points

- Accreditation of IRBs has the potential to reduce the burden of paperwork associated with conducting clinical trials. The amount of paperwork would not be reduced, but standardization would enable an IRB to work more efficiently. The ability to accept the review of other institutions participating in multicenter studies would allow investigators to spend more time working with the community.
- One purpose of accreditation would be to increase and improve the monitoring of research by IRBs. When establishing audit programs, IRBs must be careful to explain to investigators that the process is intended to assist them in conducting better research. If an appropriate rapport is established, investigators will welcome the IRBs' assistance.

DISCUSSION: PANEL I—BARRIERS TO TRANSLATING RESEARCH INTO REDUCTIONS IN THE BURDEN OF CANCER—KEY POINTS

- A strategy is needed, at the national level, to provide investigators who conduct translational research with recognition that is equal to the recognition given to those who conduct basic research.
- Experimental research exemptions would have to include rules to resolve ownership issues when an investigator invents a secondary use of a patented product.
- NCI has established a training commission to explore how to train future investigators to conduct interdisciplinary research. A conference will be held at NIH June 16–17, 2005, to discuss these issues.
- The Center for Research on Minority Health (CRMH) at the M. D. Anderson Cancer Center is a member of the Asian American Network for Cancer Awareness, Research and Training (AANCART), one of the NCI-supported Special Populations Networks (SPNs). In collaboration with the Asian American Health Coalition of Greater Houston, CRMH is bringing cancer awareness to the Asian community in that city. A survey of Chinese and Vietnamese communities has shown that 20 to 25 percent of this population is uninsured. Over 60 percent of the Vietnamese surveyed did not know where to go to find information on cancer and cancer services. The Health Coalition received a grant to conduct free mammograms for uninsured, low-income Asian women. Among almost 400 women screened, three had positive diagnoses. These women would never have known about their cancer or had the opportunity to receive treatment without this program.
- For many potential participants in clinical trials, their first encounter with the clinical research process, as well as their only orientation to that process, is being handed a 25-page consent form to complete.

- Implementation of the central IRB concept will require improved education about collaborative research for investigators, IRB members, and the community. IRBs should be able to communicate with investigators as studies are being designed, rather than simply being presented with completed applications for review.
- An IRB, like the FDA, has two roles: to promote development of new therapies and to protect the public. However, people with end-stage cancer are often more interested in access to new drugs than in human protection regulations. Participation of well-informed patient representatives on IRBs will help create a balanced analysis of the risks and benefits of new therapies.

NCI DIRECTOR'S REPORT—DR. ANDREW C. von ESCHENBACH

- In 1971, the goal of the National Cancer Act was to conquer cancer, and the means to that end was to commit the nation to an intensive research effort to understand cancer and to begin to apply what was known and what could ultimately be learned to the treatment, prevention, and detection of the disease. The NCI was empowered to oversee, coordinate, integrate, and direct the entire National Cancer Program. The effort clearly needed to focus on the front end of the continuum of discovery, development, and delivery because the fundamental mechanisms of cancer were largely unknown.
- The progress that has been made since the Act was signed has opened up an entirely new portfolio of opportunities to intervene and preempt cancer in ways that were unimaginable in 1971. Tools have become available that rapidly accelerate the pace at which progress can be made across the discovery, development, and delivery continuum. However, one can never lose sight of the fact that the endpoint of all that progress is to conquer cancer for those who are threatened and affected by the disease.
- The NCI is now focused on the full continuum of discovery, development, and delivery and has crystallized the destination for its efforts and assigned a timeline to them. The destination is not the elimination of cancer; the destination that is within reach is the elimination of the outcomes of cancer, the suffering and death that result from the complex process that is understood as cancer.
- Building on the accomplishments of the past three decades, the NCI is focusing enormous infrastructure and intellectual capital on the problem of cancer. There have never been as many investigators across the full continuum of basic, translational, clinical, and population research as there are today.
- These resources must be nurtured and expanded and—more importantly—coordinated, integrated, and applied. NCI is taking the view that its role and responsibility are not only to provide the resources necessary, but also to provide the leadership needed to nurture this effort. This applies both to areas the NCI directly controls and areas in which the Institute has influence, including other Federal agencies, the extramural community, and other outside organizations.
- A number of programs have been launched that are clearly directed towards integrative approaches to the continuum of discovery, development, and delivery. These include initiatives with the Centers for Disease Control and Prevention (CDC), FDA, and CMS. With CMS, for example, NCI is addressing enhancement of the delivery end of the continuum to ensure quality of care and adequate reimbursement so that all patients can receive the fruits of discovery and development.
- Other initiatives include caBIG, which is intended to integrate the infrastructure of Cancer Centers, and the National Advanced Technology Initiative for Cancer (NATIC), which will develop and apply the emerging technologies in genomics and proteomics and information technology and nanotechnology.
- Cancer is being used as a model for the emergence of the Department of Health and Human Services (DHHS) eHealth Initiative, which is designed to put in place an infrastructure of information technologies for management of the delivery of state-of-the-art care throughout the entire community.
- NCI also took the initiative to address the critically important problem of health disparities by serving as a model for DHHS in creating the trans-HHS health care disparities agenda.
- NCI looks forward to providing the essential and appropriate resources necessary to the discovery, development, and delivery continuum as well as providing the leadership and

integrating force that will bring together all the parts and pieces of the National Cancer Program, the purpose of which is the elimination of the suffering and death due to cancer for everyone by 2015.

PANEL DISCUSSION II—THE ROLE OF ACADEMIC MEDICAL CENTERS IN TRANSLATING RESEARCH INTO CLINICAL PRACTICE

INTRODUCTION—DR. J. CARL BARRETT

Background

Dr. Barrett is the Director of the NCI Center for Cancer Research (CCR) and Chief of the Laboratory of Biosystems and Cancer within the CCR. Previously, he was Director of the Division of Basic Sciences at NCI. Prior to coming to NCI, Dr. Barrett was Scientific Director of the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina. Dr. Barrett's research focuses on the molecular and environmental causes of cancer. As Chief of the Laboratory of Biosystems and Cancer and Head of the Cancer and Aging Section, he studies the molecular genetics of cancer and mechanisms of cancer progression. His laboratory has made several important contributions to the understanding of the mechanisms of aging and senescence of normal cells and the process of immortalization of cancer cells.

Dr. Barrett introduced the panel members.

DR. ROBERT C. BAST, JR.

Background

Dr. Bast is best known for developing the OC125 monoclonal antibody that led to the production of the CA125 radioimmunoassay. Serum CA125 levels have provided the first generally useful marker for monitoring the course of patients with epithelial ovarian cancer. CA125 is currently being evaluated as one component of a screening strategy for ovarian cancer. Dr. Bast's early studies focused on the use of immunostimulants and monoclonal antibodies for cancer therapy. Over the last 15 years, his group has pioneered definition of the molecular alterations in ovarian and breast cancers that might serve as targets for therapy as well as diagnosis. Dr. Bast's most recent studies have focused on the identification of ARHI, a novel *ras*-related tumor-suppressor gene that may prove useful for gene therapy.

Key Points

- One critical role for the academic medical center is to devise effective strategies for the prevention, detection, and treatment of cancer. Over the last two decades, the increasing understanding of cancer at the level of molecules and cells has permitted the development of targeted therapies and the promise of individualized therapy and management of cancer. Individualized management of cancer will require not only drugs, but also more novel and accurate diagnostic techniques to assess risk, detect early-stage disease, estimate prognosis, monitor tumor burden, and predict response to particular agents. Diagnostics have been a traditional strength of academia, and the academic medical center is where molecular diagnostics, molecular imaging, and molecular therapeutics can be brought together to eliminate suffering from cancer.
- There is a disconnect within medical centers between progress in the laboratory and progress in the clinic. The challenge for medical centers is to make progress in the clinic look more like progress in the laboratory by building a stronger, wider bridge between the laboratory and the clinic for "two-way traffic." The traffic on this bridge includes patients and investigators, but there are other, equally important players outside the academic medical center, including the pharmaceutical industry, FDA, and NCI.
- Traditionally, the pharmaceutical industry has come to the academic medical center relatively late in the process of drug development to conduct Phase I/II trials and, possibly,

pharmacokinetics and pharmacodynamic monitoring. With the development of targeted therapies, however, there are opportunities for new collaborations to identify relevant pathways in validating targets and developing biomarkers that predict and monitor response. NCI could support these efforts by recognizing the importance of and rewarding cancer center-industry collaborations in the context of Cancer Center Support Grant (CCSG) renewals and by facilitating the evaluation of drugs in combination, either preclinically or clinically. Most targeted therapies do not have a profound, long-term impact on human cancers; combinations of new, targeted therapies, either with each other or with more conventional drugs, will be needed to prevent and treat malignancies.

- NCI could provide a clearinghouse to facilitate the exchange of drugs across company boundaries to permit evaluation of targeted and conventional agents in combination. NCI could also provide RFAs for studies on the clinical evaluation and validation of predicted preclinical models for early clinical trials.
- FDA has placed increased emphasis on expedited review of promising antineoplastic agents. NCI should continue to encourage FDA to accept novel trial designs, particularly for Phase II studies; permit the simultaneous evaluation of drugs in combinations; and permit the use of surrogate biomarkers.
- NCI has substantially strengthened translational research in academic medical centers with training grants, SPOREs, and other funding mechanisms. Despite fiscal constraints, expansion of these programs is needed. The potential of SPORE grants to promote translational research is only now being realized; this program should be expanded to less common tumors.
- NCI can help advance molecular diagnostics and imaging by bringing together academia, diagnostic companies, NCI, and FDA to identify needs for biomarkers in the clinic and to define a paradigm for molecular biomarker development that might include novel methods of support, such as the Rapid Access to Intervention Development (RAID) program, for diagnostics. Also, diagnostic companies and academic investigators could be brought together to present novel markers developed by NCI-sponsored investigators and educate investigators regarding new approaches and platforms developed in the private sector.

Discussion: Dr. Bast—Key Points

- The primary criterion for renewal of CCSGs is the conduct of investigator-initiated, hypothesis-driven clinical trials. NCI should add collaborative work with industry to the criteria for grant renewal.
- While the SPORE program is designed to focus on cancer sites, targeted therapies may be useful for a small percentage of cancers across different cancer sites. In the future, it may be desirable to orient SPOREs around targets rather than around particular diseases. Another possibility would be to create working groups across SPOREs. M. D. Anderson has nine different SPOREs and is conducting PI3 kinase studies across several SPOREs within the institution. NCI could help by developing a matrix of SPOREs and facilitating collaboration among investigators who are working on particular targets.

DR. JACK GILL

Background

Dr. Gill is a founder and general partner of Vanguard Ventures, a venture capital firm specializing in high-technology startups, with offices in Palo Alto, California, and Houston, Texas. Vanguard manages over $500 million in capital and has been the lead investor in numerous highly successful companies, such as Aldus, Digital Microwave, Pyramid Technology,

EndoSonics, Mycogen, EndoTherapeutics, Macromedia, Network Appliance, Indigo Medical, CardioGenesis, Advanced Fibre Communications, Ciena, LightSpeed (CISCO), Tut Systems, and Digital Island. Vanguard Ventures specializes in startup investments in the computer, communications, and life sciences industries. Dr. Gill is a member of the Harvard Medical School faculty and serves on the boards of the M. D. Anderson Cancer Center, Horatio Alger Association of Distinguished Americans, Project Hope, and the Presidents' Circle of the National Academies.

Key Points

- Translating research into commercially viable and useful products is expensive and time-consuming. Bringing a medical or diagnostic device to market requires $30 to $50 million annually and 4 to 6 years. A biotechnological drug usually requires over $100 million and 4 to 8 years.
- Most funding for academic biomedical research comes from Government agencies, whereas commercialization research and development typically takes place in the private sector and in small rather than large companies. This private-sector effort creates products that go to market, improve health care, and generate jobs, exports, and taxes.
- Most intellectual property is generated by academic researchers and independent inventors who have no business experience. Venture capitalists and other investors are needed to help them develop ideas into practical products. They often have trouble working with people they perceive as having inflexible egos and naïve or unrealistic expectations. The typical process of matching a technical team with a business interest, determining the viability of a product concept, and developing a business plan takes about $1 million and about 12 months. This process is worthwhile to venture capitalists because the worldwide market for drugs is about $400 billion, and for devices and diagnostics, about $200 billion.
- Academic medical centers need to develop better-organized processes for starting commercial enterprises. Academic institutions should be establishing technology transfer departments and developing policies and procedures related to intellectual property issues. Scientists and engineers who also have business experience must be involved in this process. The final step is to provide "gap funding" to support development of ideas that are not yet ready for the involvement of venture capitalists.

Discussion: Dr. Gill—Key Points

- The Harvard-MIT Center for the Integration of Medicine and Innovative Technology (CIMIT) makes funds available for collaborative projects in interventional medicine. In its 6 years of existence, the program has raised about $100 million.
- Foundations that raise money for cancer research should be encouraged to become involved in providing the gap funding needed to bring ideas to the point at which they are ready for business plan development.

DR. ANTHONY INFANTE

Background

Dr. Anthony Infante, M.D., Ph.D., is Professor of Pediatrics and Microbiology and Immunology and Associate Dean for Research at the Medical School of the University of Texas Health Sciences Center at San Antonio. He served as Head of the Division of Pediatric Hematology/Oncology/Immunology from 1994 to 2001 and as interim Director of the Children's Cancer Research Institute from 1999 to 2002. He became the Medical School's first Associate Dean for Research in 2000. Dr. Infante's current research focuses on the expression, development, and function of T-cell receptors in the immune systems of children with immune

deficiency disorders. He practices medicine as Director of the Children's Immunology Clinic at CHRISTUS Santa Rosa Children's Hospital in San Antonio.

Key Points

- Minority-Based Community Clinical Oncology Programs (MBCCOPs) enroll patients into NCI-supported clinical trials as an important means of providing patients with access to state-of-the-art therapies. There is a vast cultural difference between academic physicians and private-practice physicians, and it takes a long time to build the communication and mutual trust on both sides needed to bring private practitioners into MBCCOPs. Reaching the goals of the program requires listening to both the participating physicians and patients.
- The South Texas Pediatric MBCCOP has built continuous quality improvement into its program. One example of this grew out of frustration at the typical inability of Cooperative Groups to provide "cancer control credits" for pediatric patients. By looking at the incidence of obesity and diabetes in childhood cancer survivors, it was noticed that childhood leukemia survivors have higher-than-normal rates of obesity; this may have something to do with exposure to glucocorticoids during treatment. The South Texas Pediatric MBCCOP is working with local diabetes experts to address this problem.
- Other problems faced by programs working with minority patients are cultural differences that affect health-related behavior and create problems with the informed consent process. Academic medical centers need to improve their efforts to provide patients with the information they need to understand clinical protocols.

Discussion: Dr. Infante—Key Points

- The MBCCOP grant primarily pays for clerical support and the work of research nurses. Most of the cost of data management is covered by funding for other research projects.
- The field of pediatrics has a strong tradition of supporting clinical research. This has made the task of establishing trust between researchers and private physicians somewhat less difficult than in other disciplines.

DR. LYNN MATRISIAN

Background

Dr. Matrisian is Professor and Chair of the Department of Cancer Biology and Ingram Professor of Cancer Research at Vanderbilt University School of Medicine. She is the Program Leader of the Host-Tumor Interaction Program at the Vanderbilt-Ingram Cancer Center, a member of the Board of Scientific Advisors of the National Cancer Institute, and President of the American Association for Cancer Research. Dr. Matrisian has served as a member of the NCI Pathology B Study Section, NIH, and associate editor of several cancer journals. She has organized several national and international scientific conferences and is a cofounder of the Protease Consortium. Her research interests revolve around the molecular mechanisms underlying tumor progression and metastasis, with emphasis on the biology of matrix-degrading proteinases.

Key Points

- Academic medical centers provide an opportunity for real transformational advances in translational research, not only because they bring together basic science and patient care, but also because of their educational mission, which is sometimes undervalued in looking at this problem. Encouraging translational science in the academic setting will make it easier to train the next generation to become effective translational researchers. This can be accomplished by realigning the reward system to promote multidisciplinary research.