Board of Scientific Advisors

Meeting Minutes

March 3-4, 2003

Conference Room 10, C Wing, Building 31
Bethesda, Maryland 20892

Quick Links

Members

Agenda & Future Meetings

Meeting Minutes

BSA: Page 1

The Board of Scientific Advisors (BSA or Board), National Cancer Institute (NCI), convened for its 23rd regular meeting on Monday, March 3, 2003, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Frederick Appelbaum, Director, Clinical Research Division, Fred Hutchinson Cancer Research Center, presided as Chair.

The meeting was open to the public from 10:45 a.m. until 6:15 p.m. on 3 March for opening remarks from the Chairman; ongoing and new business; the National Cancer Advisory Board's (NCAB) P30/ P50 Working Group report; a Working Lunch featuring the P01 workload; and new and reissued Request for Applications (RFAs) concepts and Cooperative Agreements (Coop. Agr.). From 8:30 a. m. on Tuesday, 4 March, until adjournment at noon, the Transdisciplinary Tobacco Use Research Centers (TTURCs) conducted a series of mini-symposia, and the Division of Cancer Control and Population Sciences (DCCPS) presented program status reports.

Board Members present:
Dr. Frederick R. Appelbaum (Chair)
Dr. David B. Abrams
Dr. David S. Alberts
Dr. Hoda Anton-Culver
Dr. Esther H. Chang
Dr. Thomas Curran
Dr. Raymond Dubois
Dr. H. Shelton Earp III
Dr. Patricia Ganz
Dr. Susan B. Horwitz
Dr. Hedvig Hricak
Dr. Eric Hunter
Dr. William G. Kaelin, Jr.
Ms. Paula Kim
Dr. Kenneth W. Kinzler
Dr. Herbert Y. Kressel
Dr. Michael Link
Dr. Lynn Matrisian
Dr. W. Gillies McKenna
Dr. Christine A. Miaskowski
Dr. Enrico Mihich
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Mack Roach III
Dr. Richard L. Schilsky
Dr. Margaret Spitz
Dr. William C. Wood
Dr. Robert C. Young

Board Members absent:
Dr. Neil J. Clendeninn
Dr. Ellen V. Sigal
Dr. Mary Beryl Daly

NCAB Liaison:
TBN

Others present: Members of NCI's Executive Committee (EC), NCI Staff, Members of the Extramural Community, and Press Representatives.

TABLE OF CONTENTS

I. Call to Order and Opening Remarks; Dr. Frederick Appelbaum
II. Consideration of 14-15 November 2002 Meeting Minutes; Dr. Frederick Appelbaum
III. Ongoing and New Business; Dr. Frederick Appelbaum
    - ASTRO "NCI Listens" 2002 Report; Dr. W. Gillies McKenna
    - BSA at National Meetings - 2003 Sessions: SBM, AACR, ONS; Dr. Frederick Appelbaum
    - Other Issues
IV. NCAB P30/P50 Working Group Report - Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future; Dr. Joseph Simone
V. Working Lunch

- P01 Workload; Dr. Marvin Kalt

VI. RFA/Cooperative Agreements New Concepts; Presented by NCI Program Staff

Division of Cancer Treatment and Diagnosis; Dr. Malcolm Smith

- Academic Public - Private Partnership Program (Coop. Agr.)/Academic Public-Private Partnership Planning Grant (RFA); Dr. Edward Sausville
- Consortia for Clinical Development of Molecular Profiles in Cancer (Coop. Agr.); Drs. James Jacobson and Barbara Conley

Division of Cancer Control and Population Sciences

- Understanding Mechanisms of Physical Activity Behavior Change (RFA) ; Dr. Louise Mâsse

VII. RFA/Cooperative Agreements Reissuance Concepts; Presented by NCI Program Staff

Division of Cancer Treatment and Diagnosis; Dr. Malcolm Smith

- Division of Cancer Treatment and Diagnosis Pediatric Brain Tumor Consortium (Coop. Agr. Re-issue); Dr. Malcolm Smith

Division of Cancer Prevention

- Community Clinical Oncology Program (CCOP)/ Minority-Based Clinical Oncology Prog. (MBCCOP) (Coop. Agr. Re-issue); Drs. Leslie Ford and Lori Minasian
- Early Detection Research Network (EDRN) (Coop. Agr. Re-issue); Drs. Peter Greenwald, Sudhir Srivastava, and Bernard Levin

VIII. Ongoing and New Business II; Dr. Frederick Appelbaum

IX. Mini-Symposia: Transdisciplinary Tobacco Use Research Centers (TTURCs)

- Introduction; Dr. Robert Croyle
- Description of TTURC Initiative; Dr. Scott Leischow
- Vectors of Tobacco Use Vulnerability in Adolescents and Young Adults; Dr. Frances Leslie
- Transdisciplinary Tobacco Use Research Centers: A New Model for Translational Research; Dr. Thomas Glynn

X. Division of Cancer Control and Population Sciences:

Program Status Reports

- Introduction; Dr. Robert Croyle
- Update of Studies of Breast Cancer on Long Island; Dr. Deborah Winn
- Cancer Intervention and Surveillance Modeling Network (CISNET); Dr. Eric Feuer
- Improving the Quality of Cancer Care; Dr. Joseph Lipscomb

I. CALL TO ORDER AND OPENING REMARKS - DR. FREDERICK APPELBAUM

Dr. Appelbaum called to order the 23rd regular meeting of the BSA and welcomed members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Appelbaum welcomed new members, Dr. Eric Hunter, Director, Center for AIDS Research, University of Alabama, and Dr. Mack Roach III, Professor in Residence, University of California, to the Board. He reminded Board members of the conflict-of-interest regulations and confirmed future meeting dates through November 2005.

top

II. CONSIDERATION OF THE 14-15 NOVEMBER 2002 MEETING MINUTES - DR. FREDERICK APPELBAUM

Motion: The minutes of the 14-15 November 2002 meeting were unanimously approved.

top

III. ONGOING AND NEW BUSINESS I - DR. FREDERICK APPELBAUM

Dr. Appelbaum indicated that Dr. von Eschenbach would give a presentation at the American Society of Preventive Oncology (ASPO) meeting to be held 9-11 March 2003 in lieu of an "NCI

Listens" session.

ASTRO "NCI Listens" 2002 Report

Dr. Gillies McKenna, Henry K. Pancoast Professor and Chair, Department of Radiation Oncology Hospital of the University of Pennsylvania, reported that Drs. Norman Coleman, Paulette Gray, and Daniel Sullivan participated in the "NCI Listens" session at the American Society for Therapeutic Radiology and Oncology (ASTRO) meeting in October 2002. The reorganization of NCI's Radiation Oncology Sciences Program was presented. A concern raised during the session was that training programs in radiation biology that cover the full spectrum of radiation effects on biological tissues have been disappearing. These programs were established in the aftermath of World War II and began to be dismantled at the end of the Cold War. The result is that there is less-than-adequate training in radiology and radiation oncology and inappropriate application of radiation in cancer research. Another concern identified was the high probability of mass radiation exposure in the United States within the next decade due to the detonation of a thermonuclear device. To determine the severity of the lack of radiation biology training programs and to recommend possible solutions, Dr. Coleman agreed to establish a task force with ASTRO, the Radiation Research Society, and NCI.

BSA at National Meetings-2003 Sessions: SBM, AACR, ONS

Members and staff representing the BSA during "NCI Listens" sessions at upcoming annual national meetings are:

- **Society of Behavioral Medicine (SBM):** March 19-22, 2003, Salt Lake City, UT; Drs. David Abrams (Chair), Robert Croyle, Paulette Gray, and Vish Viswanath.

- **American Association for Cancer Research (AACR):** April 4-11, 2003, Toronto, Ontario, CAN; Drs. Hoda Anton-Culver (Chair), Anna Barker, Thomas Curran, Shelton Earp III, Ellen Feigal, Paulette Gray, Enrico Mihich, Dinah

Singer, and Carolyn Strete.

- **Oncology Nursing Society:** May 1-4, 2003, Denver, CO; Drs. Christine Miaskowski (Chair) and Robert Croyle, Paulette Gray, Ms. Paula Kim, and Ms. Mary McCabe.

Other Issues

Dr. Appelbaum informed the Board that the subcommittee, Drs. Nancy Mueller (chair), Enrico Mihich and Robert Young, established to review the Cancer Genetics Network (CGN) will present a progress report at the June 2003 BSA meeting. If the subcommittee recommends reissuing the concept, it will be presented at the November 2003 meeting.

top

IV. NCAB P30/P50 WORKING GROUP REPORT - ADVANCING TRANSLATIONAL CANCER RESEARCH: A VISION OF THE CANCER CENTER AND SPORE PROGRAMS OF THE FUTURE - DR. JOSEPH SIMONE

Dr. Joseph Simone, President, Simone Consulting, presented the ad Hoc NCAB P30/P50 Working Group report which he and Dr. Arthur Nienhuis co-chaired. Dr. Simone informed members that the Working Group was charged by Dr. von Eschenbach to determine how to maximize translational research, suggest priorities under tight budgets, explore incentives to leverage NCI support with other partners, suggest mechanisms for Cancer Centers and Specialized Programs of Research Excellence (SPOREs) to play a greater role in NCI's agenda, and recommend 5-year goals and measures of progress. Members were told that the SPORE program (P50 award mechanism) was established in 1992 to promote and support translational research. The program's focus has been on specific disease sites. Forty-one of the 44 SPOREs are in NCI-designated Cancer Centers. He noted that the P30 award mechanism, a Cancer Center Support Grant (CCSG), funds infrastructure for cancer programs rather than research. There are 61 basic, clinical, and comprehensive Cancer Centers. Dr. Simone

informed members that the Working Group addressed the current structure of the P30 and P50 programs; their guidelines and goals; better ways to coordinate the two programs; leveraging strategies for P30s to attract other support; potential expansion of P30s' roles in their regions; flexibility of the P30 budget for research innovations; improvement of networks; and measures of progress.

Consensus was reached on several basic findings: 1) the Cancer Centers program is strong; 2) Centers are the sites in which most translational and other cancer research is conducted in the United States; 3) approximately 50 percent of NCI's extramural funding is allocated to Cancer Centers; 4) with mandates and resources, their infrastructure can be adapted to embrace novel programs; 5) a typical P30 award receives approximately $2M annually in direct costs, $55M in grants, $1.5M in institutional money, and $3M in gifts; 6) the integration of Cancer Centers with SPOREs, however, is spotty; 7) the guidelines limit innovation and flexibility; 8) there is no credit given in the assessment of P30s for community outreach or cooperative group participation; and 9) the review process is excessively long and needs updating.

Basic findings on SPOREs indicate that: 1) the program is very popular with both participants and advocates; 2) there is active communication among SPORE members; 3) it's too early to evaluate its effectiveness and/or the need for structural evolution; 4) its growth rate is swift and not sustainable in the current financial climate; and 5) the review process needs adjusting.

The Working Group's three major recommendations, accompanied by seventeen implementation suggestions, were presented: First, Cancer Centers and SPOREs are vital components of NCI's translational research efforts and must be sustained, even in the current challenging financial environment. Suggestions to accomplish this recommendation include: a) stretching the funding by limiting P30 growth to just above the level of R01s and suspending the ineffective P20 planning grant mechanism; and b) slowing down P50 growth to equal that of R01s by reducing the average dollar amount per grant, sharing resources with P30s, and requiring non-Federal matching funds.

Second, better use of Cancer Centers as entrepreneurial resources for planning, innovation, and dissemination is urged. Suggestions to accomplish the recommendation include: a) regularly involving

Cancer Center directors in NCI's strategic planning, developing new initiatives and holding annual meetings with NCI top executives; b) use existing Cancer Centers resources as cost-effective sites for piloting new research and establishing dissemination programs; c) allowing salary support in the P30s for clinical trial physicians as essential research resources; d) revising the dollar allowance for critical, under-, and nonfunded resources, such as tissue banks, data systems, and regulatory compliance; e) spreading the Cancer Centers program through a new funding mechanism for academic institutions or programs that undertake cancer research activities but do not qualify for P30s to partner with existing P30s; f) providing support through the P30 mechanism to Cancer Centers establishing collaborations with state agencies, health departments, and the Centers for Disease Control and Prevention (CDC), etc.; and g) modifying the P30 award to encourage novel methods and infrastructure to disseminate new knowledge in early detection, prevention, cancer control, and clinical research.

Third, NCI should make a concerted effort to improve efficiency, effectiveness, and evaluation of Cancer Centers and SPOREs. To implement this recommendation, the NCI should: a) catalyze, as a top priority, the development of an integrated national clinical research informatics system; b) limit or omit the added layer clinical trials review that have already been peer reviewed; c) work with the Office for Human Research Protections (OHRP) to develop a centralized Institutional Review Board (IRB) for multicenter clinical trials; d) streamline the P30 review process by eliminating some site visits; e) consider and weigh for P30 review the Cancer Center's activities with P50s, cooperative groups, and networks, as well as with community outreach, service, and dissemination; f) initiate a planning process to develop quantifiable metrics determining the size of P30 awards that reflect the broad impact of Cancer Centers; g) employ a two-tiered system of SPORE review with a parent committee to review applications across tumor sites to better manage the program; and h) develop an annual process to describe and measure the overall contributions of both the P30 and P50 programs, including attracting non-Federal funds, training, and impact of regional collaborations.

The Working Group concluded that:1) Cancer Centers and SPORE-like activities are vital to NCI's translational, basic, and clinical research efforts; 2) the programs should be sustained, with

revisions to improve their efficiency and effectiveness; and 3) NCI should adjust the P30/P50 programs to reflect budget constraints, but should remain poised to do more when the dollars increase in the future.

In discussion, the following points were made:

- Potential interface between Cancer Centers and SPOREs should be based not only on disease site but also on molecular target specificity across cancer sites.

- While Cancer Centers are interested in conducting community outreach, and patients and the advocacy community view these Centers as enhancing quality of care, there is no funding mechanism to support these activities within the Cancer Centers.

- Dissemination activities and research are poorly funded in the core grant for Cancer Centers. Dissemination of new knowledge should be a priority in the P30 funding mechanism.

- SPOREs should be required to have matching funds and/or show evidence of support from an academic institution, philanthropic organization, etc. that would benefit from partnering.

top

V. WORKING LUNCH

P01 Workload

Proposed Changes in the Peer Review System for Program Project Grants. Dr. Marvin Kalt, Director, Division of Extramural Activities (DEA), NCI, noted that the doubling of the NIH budget has encouraged the submission of additional investigator-initiated research applications. The NCI has been receiving annually about 105 to 110 new, competing continuations, and amended Program

Project (P01) applications. Future years projections indicate that 120 to 130 P01 applications will be received each year. Additionally, the total number of active P01s fluctuates between 185 and 195. Since most are funded for 5 years, there is a 20 to 25 percent turnover per year in Type 5s, although they are not evenly spaced out across all award periods.

The review process is labor-intensive and most original applications require a site visit. Applications are referred to three parent committees focusing on basic, clinical, and population-based sciences. Because the rate of researchers becoming full professors is slower than the rate of submission of new grant applications, lack of availability of peer reviewers is becoming a major barrier to the NCI's ability to handle the workload. The NCI has begun to examine models that might reduce the workload intensity for both reviewers and staff without negatively affecting the outcome. Proposed models, which would still be based on a two-tiered system but would reduce the number of site visits are: 1) ad hoc reviewers and members of the parent committee with appropriate expertise would review paper copies of applications and participate in teleconferences with applicants; 2) cluster reviews, in which small groups of applications with overlapping scientific objectives would be assigned to reviewers with similar expertise. Again, teleconferencing would be used in place of a site visit prior to bringing the applications before the parent committee; and 3) elimination of site visits which would decrease the total number of reviewers required. Members were told that the NCI is interviewing peer reviewers, as well as past, present, and future P01 grantees, to solicit their input on these ideas. Further reports will be presented to the BSA at future meetings.

In discussion, the following points were made:

- An adequate pool of peer reviewers is affected by increasing collaboration among NCI grantees, which increases levels of conflict of interest. In addition, NCI advisory board members and intramural scientist are prohibited from serving on peer-review panels.

- The NCI should explore ways to encourage successful grantees to participate in the peer-review process. Cancer Centers should be required to provide lists of staff who are qualified to serve as reviewers.

- Consideration should be given to changing the term of service on a parent committee from 4 to 3 years.

- The guidelines and amount of information requested for applications should be simplified to reduce the workload for applicants

top

VI. RFA/COOPERATIVE AGREEMENTS NEW CONCEPTS - PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Treatment and Diagnosis

Academic Public-Private Partnership Program (Coop. Agr.)/ Academic Public-Private Partnership Planning Grant (RFA). Dr. Edward Sausville, Associate Director, Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis (DCTD), NCI, stated that the purpose of the Academic Public-Private Partnership Program (AP4) is to stimulate cancer intervention discovery and development research at academic centers in partnership with industry, nonprofits, and government. The proposal will focus on incorporating the latest technologies to find novel, mechanistically targeted drugs for underserved diseases and supporting the necessary expertise to reduce the time required to translate new drug discoveries into therapies.

Dr. Sausville informed members that the idea for the AP4 concept, a new drug discovery and development assistance program, was modeled after the National Science Foundation's Industrial/ University Cooperative Research Centers. Each AP4 Center would have an Academic Director, partners with other academics and representatives from the pharmaceutical and biotechnology industries and nonprofits, be governed by a Steering Committee that would include a nonvoting NCI representative. The Director would use a one year planning grant to conceive a partnership and identify partners, then generate a governance document to define

the financial contributions, interactions, intellectual property issues, and expectations of each partner. The Director would then administer subsequently approved program grant applications. He noted that dynamic program and project management is a key feature of the concept.

AP4 evaluation metrics, including the characterization of cancer-relevant targets and communication between and contributions from partners and more traditional endpoints, were described. Dr. Sausville estimated that 10 to 15 planning grants would be accepted from 40 to 60 applications. Of these, six partnerships would be approved for funding. Three would receive $450,000/year directly from NCI, with a minimum of $300,000 (total) from the partners. The other three partnerships would receive $600,000/year from NCI, with $450,000 from the partners. This level of funding would be solid for 3 years, and NCI's contribution would be scaled down for the final 2 years.

The proposed length of the planning grant award for this one-time solicitation is 1 year at a total cost of $1.125M for an estimated 15 U56s. The proposed length of the program grant award for this one-time solicitation is 5 years, with a first year set-aside of $4.725M and a total cost of $19.731M for an estimated 6 U54s.

In discussion, the following points were made:

- The proposed one year duration of the planning grant may not be adequate to negotiate intellectual property issues and agreements from multiple industrial partners.

- Rather than fund all the grants at once, it may be more effective to stagger them to ensure the best potential products and partnerships.

Motion. A motion to approve the DCTD Cooperative Agreement RFA concept entitled "Academic Public-Private Partnership Program" passed with 25 in favor and 1 abstention. Status reports should periodically be given to the Board. The concept should be returned to the BSA prior to any reissuance.

Motion. A motion to approve a DCTD RFA concept entitled "Academic Public-Private Partnership Planning Grant" at the time

specified in the proposed concept passed with 24 in favor; 1 against; and 2 abstentions.

Consortia for Clinical Development of Molecular Profiles in Cancer (Coop. Agr.). Dr. James W. Jacobson, Chief, Technology Development Branch, Cancer Diagnosis Program (CDP), DCTD, NCI, explained that the process of moving from discovery to development is difficult, time-consuming, and expensive. Dr. Jacobson stated that the Director's Challenge RFA addressed identifying new profiles and will be replaced by the proposed initiative for the clinical evaluation of profiles. Two particularly successful gene expression-profiling collaborations with clinical relevance were highlighted. He noted that the Director's Challenge programs are not structured for clinical development, but that the new Consortia might generate patient benefit from rigorous clinical evaluation.

Dr. Barbara Conley, Chief, Diagnostics Research Branch, CDP, DCTD, NCI, emphasized the importance of generating confidence that a particular diagnostic assay is reliable and robust before bringing it into clinical use. The population of interest and eligibility criteria must also be considered, as must clinical benefit. Technology modification and adaptation, rather than development, is the focus of this initiative. Applicants must demonstrate analytical proficiency, as well as appropriate statistical design, specimen resources, and multidisciplinary expertise. A Steering Committee, composed of the Principal Investigator, NCI staff, and one member from each funded application, will address issues and problems that affect all the projects. Applicants will be required to make the data publicly available and to address intellectual property issues. NCI staff will assist grantees with the initiation of clinical trials. An external Advisory Board will advise the Steering Committee and help evaluate progress.

The proposed length of award for this one-time solicitation is 5 years, with a first year set-aside of $10M and a total cost of $50M for an estimated three to four U01s.

In discussion, the following points were made:

- Additional consortia may "fragment" resources and duplicate infrastructure; partnering with other initiatives

may be more cost-effective. Scientific objectives might be accomplished with competitive supplements to existing structures rather than creating a new RFA.

- It may be premature to identify 3 or 4 targets that warrant a $12M investment over 5 years. Initial profiles must be ready at time of grant application.

- The timeframe proposed for preparing the application may not allow enough time between grant announcement and submission date.

Motions. A motion to approve a DCTD Cooperative Agreement RFA concept entitled "Consortia for Clinical Development of Molecular Profiles in Cancer" was defeated with 3 in favor; 25 opposed.

Motion. A motion to form a subcommittee to work with NCI staff to revise the DCTD Cooperative Agreement RFA concept entitled "Consortia for Clinical Development of Molecular Profiles in Cancer" passed unanimously. Subcommittee members are Drs. John Minna (Chair), Hoda Anton-Culver, Esther Chang, Tom Curran and Richard Schilsky. With the subcommittee's concurrence, the revised concept will be presented at the next BSA meeting.

Division of Cancer Control and Population Sciences

Understanding Mechanisms of Physical Activity Behavior Change (RFA). Dr. Louise Mâsse, Health Promotion Research Branch (HPRB), Behavioral Research Program, DCCPS, NCI stated that the purpose of this concept is to increase the knowledge base necessary to develop effective physical activity interventions. Lack of physical activity and obesity (which may itself be due to lack of physical activity) have been linked to an increased risk for certain cancers. However, the benefits of physical activity extend beyond cancer risk prevention, i.e., exercise by cancer patients before, during, and after treatment provides prevention, buffering, and coping effects. Despite the health effects of physical activity, American adults achieve less than 25 percent of the target level of activity recommended in the Healthy People 2010 national health agenda. To increase the pace of physical activity intervention

research, an understanding of how behavior is changed must be developed. The proposed multidisciplinary approach will help assess psychosocial, environmental, and biological factors that affect behavior.

Dr. Mâsse described the weaknesses in the current NIH research portfolio in relation to studies of physical activity behavior modification. She noted that the concept should garner support across NIH Institutes, fits well within the mission of the Office of Cancer Survivorship and the HPRB, and is a Department of Health and Human Services (DHHS) priority.

The proposed length of the award for this one-time solicitation is 2 to 5 years, with a first year set-aside of $1.75M and a total cost of $8.75M for an estimated 6 to 10 awards (R01 or R21).

In discussion, the following points were made:

- Genetic predisposition should be included in the study, as well as modifiers such as ethnicity, gender, age, and socioeconomic status.

- Concerns were voiced about the low funding budget. Partnering with other organizations is encouraged to increase funding.

Motion. A motion to approve the DCCPS RFA concept entitled "Understanding Mechanisms of Physical Activity Behavior" passed with 22 in favor, 5 against, and 1 abstention. Board members suggested that controls for diet, genetic components, and other moderators be added. Additionally, funding should be increased by partnering with other organizations.

top

VII. RFA/COOPERATIVE AGREEMENTS REISSUANCE CONCEPTS- PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Treatment and Diagnosis

Pediatric Brain Tumor Consortium (Coop. Agr. Reissue). Dr. Malcolm Smith, Head, Pediatric Section, Cancer Therapy Evaluation Program (CTEP), DCTD, NCI, reminded the Board that brain tumors are the most common cause of cancer-related mortality in children. He summarized the purpose of this concept as promoting multi-institutional collaborations necessary for studying the infrequent and varied types of pediatric brain cancers. The Pediatric Brain Tumor Consortium (PBTC) uniquely provides neurological expertise to clinical trials of pediatric brain tumor treatments and therefore distinguishes its activities from those of the Children's Oncology Group (COG). While the NCI supports brain tumor research through several funding mechanisms (Cooperative Agreements, Program Projects, SPOREs, Centers, R01s, R21s, and small business grants), only the PBTC has focused on multi-institutional, early-phase pediatric neuro-oncology clinical trials.

In his review of the establishment of the PBTC, Dr. Smith emphasized the extraordinary expertise represented in the membership, the Consortium's well-developed infrastructure, the extensive linkages with the pharmaceutical and biotechnology industries, interactions with COG, and a state-of-the-art data management system. In particular, the PBTC has developed and implemented a secure Internet-based electronic infrastructure for imaging transfer using both NCI funds and contributions from private foundations.

Dr. Smith informed members that PBTC successes, since its inception in 1999, include 10 approved protocols, with an average of 100 patients enrolled into clinical trials each year. He provided examples of two studies orchestrated by the PBTC that would not otherwise have been conducted: (1) the PBTC-001 Protocol and (2) the PBTC-011 Phase I/II trial. He noted that future research by the PBTC falls under three areas of research priority: 1) completing studies on convection-enhanced delivery and building upon pilot studies of local delivery approaches; 2) improved efficacy of intrathecal therapies; and 3) the integration of biological characterizations and preclinical drug testing into the selection of molecularly targeted agents for study in children with brain tumors. Dr. Smith outlined criteria for success at the end of the 5-year funding period and noted that the PBTC has successfully developed the infrastructure to accomplish technically challenging pediatric brain tumor protocols. Moreover, the PBTC has met the protocol

and accrual targets in the initial RFA.

The RFA reissuance would support a single application solicitation from the PBTC Operations and Biostatistics Center (OBC) with subcontracts to member institutions and be equal in funding to the total of current awards to the PBTC OBC and the nine member institutions. The proposed length of award for this one time letter RFA reissuance cooperative agreement solicitation is 5 years, with a first-year set-aside of $2.5M and a total cost of $12.75M.

In discussion, the following points were made:

- In retrospect, it might have been appropriate to build the functions of the PBTC within the COG infrastructure, although the responsibilities currently managed by the PBTC could not readily be assumed by COG at this point. The Board will reassess the independence of the PBTC within 2 years.

- PBTC's expertise in electronic imaging transfer should be exported to larger Cooperative Groups that have been grappling with this issue.

- Follow-up data on adoptive transfer therapy have been collected for only 2 years. Long terminformation needs to be obtained to ensure that the transferred T cells do not mutate and result in a lymphoma or leukemia. A fail-safe mechanism may need to be added to this type of immunotherapy.

Motion. A motion to concur with the NCI decision to reissue the DCTD Letter Cooperative Agreement RFA concept entitled "Pediatric Brain Tumor Consortium (PBTC)" was approved with 26 in favor and 1 abstention. In two years, a plan should be brought to the Board indicating what will happen in five years, that is, whether the PBTC 1) is going to continue as an independent Cooperative Group, 2) will be another RFA reissuance, or 3) will be folded into the existing Cooperative Group structure.

Division of Cancer Prevention

Community Clinical Oncology Program (CCOP)/Minority-

Based Clinical Oncology Program (MBCCOP) (Coop. Agr. Re-issues). Dr. Leslie Ford, Associate Director, Clinical Research, Division of Cancer Prevention (DCP), NCI, introduced the CCOP as a 20-year-old endeavor that has become an ongoing NCI program with an annual release of the RFA. Dr. Ford informed members that the CCOP is an integral component of NCI's Clinical Trials Network and supports research and dissemination of state-of-the-art cancer care. The MBCCOP, an important focus of the CCOP, specifically addresses access to clinical trials research by minority populations. The purpose of the concept is to continue developing the CCOP network as a national resource providing support for: (1) community oncology physicians to enter patients into NCI-sponsored clinical trials; and (2) Research Bases to design, develop, and conduct cancer prevention and control clinical trials. She announced the intention to develop standing guidelines for the CCOP and schedule annual program announcements such that new applicants could become involved with the CCOP.

Major accomplishments of the CCOP include the involvement of community oncologists as equal partners in research; establishment of a research network that extends beyond medical oncologists; development of a successful mechanism for complementing landmark prevention trials; and expanding the scientific purview of Research Bases, such as the Cooperative Groups and Cancer Centers, to include rigorous research in cancer prevention and control.

Dr. Lori Minasian, Chief, Community Oncology and Prevention Trials Research Group (COPTRG), DCP, NCI, highlighted the program's structure and detailed CCOP's accomplishments. Dr. Minasian reported that the current NCI portfolio consists of 50 CCOPs, 11 MBCCOPs, and 12 Research Bases. More than 400 hospitals and 4,000 physicians participate in the CCOPs. As a direct result of CCOPs increased funding, accrual to clinical trials has risen steadily in the past 5 years. In parallel, cancer control credits have increased due to the availability of cancer prevention and control trials. Additionally, more than 92,000 patients have enrolled in treatment clinical trials. CCOP's impact on cancer prevention and control cannot be measured as concretely as that on cancer treatment. A broad portfolio of clinical trials and ongoing programs designed to manage cancer symptoms and reduce morbidity were described.

The proposed length of award for both the CCOP and MBCCOP RFA reissuance solicitations is 3 to 5 years, with first-year set-asides of $9.5M and $1.9M and a total cost of $44.3M and $8.7M, respectively. The estimated number of cooperative agreement awards is 15 (U10) for the CCOP and 5 (U10) for the MBCCOP.

In discussion, the following points were made:

- Twenty Year CCOP/MBCCOP Evaluation Report should be given at a future BSA meeting.

Motion. A motion to concur with the NCI decision to reissue DCP Cooperative Agreement RFA concepts entitled "Community Clinical Oncology Program (CCOP)" and "Minority-Based Clinical Oncology Program (MBCCOP)" and annual reissuances for 5 years was unanimously approved.

Early Detection Research Network (EDRN) (Coop. Agr.). Dr. Peter Greenwald, Director, DCP, NCI, defined the EDRN as a flagship NCI program and emphasized the crucial nature of the development and validation of biomarkers. He introduced Drs. Sudhir Srivastava and Bernard Levin.

Dr. Srivastava, Chief, Cancer Biomarkers Research Group, DCP, NCI, stated that in its 3 years of existence, the EDRN had: 1) established an infrastructure that provides a collaborative platform for translational research bridging discovery and validation studies; 2) developed many useful informatics tools, including the "EDRN Information Exchange," which enables seamless integration with various other Web sites around the country, and a Web-based portal for sharing, exchanging, and depositing data; 3) defined a number of candidate biomarkers; 4) defined a five-phase approach to biomarker discovery and validation; 5) developed a resource for non-EDRN members; and 6) established an active public Web site for communicating and disseminating information and 7) begun to jointly sponsor a Gordon Research Conference: "Frontiers in Cancer Detection and Diagnosis." Dr. Srivastava concluded by reviewing the benefits of renewing the EDRN RFA.

Dr. Levin, Division of Cancer Prevention, M. D. Anderson Cancer Center, offered comments from the Network Consulting Committee (NCC), which advises the EDRN Steering Committee

and is composed of non-EDRN members. Dr. Levin stated that the Committee believes significant progress had been achieved in addressing the goals of the EDRN in the areas of scientific excellence, collaborations, and communications. The EDRN infrastructure provides valuable service to the scientific community in biomarker development and evaluation. Importantly, the EDRN has developed significant interactions with clinical and basic scientists.

His recommendation was that the NCC should continue and financial support should increase. Dr. Levin indicated that NCC members expect more collaborative validation studies in the coming years and would like to see the EDRN become an ongoing program with increased visibility in order to enhance collaborations and solicit industrial partnerships. The rationale for the NCC recommendations includes the awareness that investigator-initiated research has failed to provide any validated markers; the scope of collaborations in the EDRN is unlikely to be achieved by other means; esearch investments can be maximized long-term with the EDRN; and, at this time of limited resources, the EDRN helps contain costs. Moreover, the EDRN offers an opportunity for both public and private partnerships.

The budget for the EDRN uses a staggered funding approach over a period of 7 years. The first-year set-aside for this one time RFA reissuance solicitation is $13M, with a total cost of $173M for an estimated 30 cooperative agreement (U01 or U24) awards. [Budget approved for 5 years instead of the requested 7 years.]

In discussion, the following points were made:

- Identification of clinically useful markers cannot be expected at this point due to the EDRN's short development period.

- The rationale for maintaining 18 development laboratories to define potential biomarkers was questioned, since the bottleneck for discovery of clinically useful markers occurs at validation. More funding should be provided to validate biomarkers rather than discover more potential biomarkers.

Motion. A motion to concur with the NCI decision to reissue the

DCP Coop. Agr. RFA entitled "Early Detection Research Network (EDRN)" was approved with 18 votes in favor, 7 abstentions, and 2 opposed. Board members approved a 5-year rather than a 7-year funding period. Furthermore, Board members recommended reducing the emphasis on development laboratories and increasing the emphasis on validation laboratories.

top

VIII. ONGOING AND NEW BUSINESS II - DR. FREDERICK APPELBAUM

Dr. Appelbaum presented for consideration by the full Board the suggestion of limiting NCI staff concept presentations to 15 minutes and allowing 45 minutes for subsequent discussion of each concept. He also suggested placing the review of concepts earlier on the agenda, especially if they involve a high level of funding. Since Board members receive the written reports of concepts to be reviewed at a BSA meeting ahead of time, it was suggested that hard copies of the slide presentations be attached to the reports. Dr. Gray indicated that if the slide presentations are available at the time of submission, they will be included with the reports.

top

IX. MINI- SYMPOSIA: TRANSDISCIPLINARY TOBACCO USE RESEARCH CENTERS (TTURCs)

Introduction. Dr. Robert Croyle, Acting Director, DCCPS, NCI, briefly described the scientific research and initiatives undertaken by the DCCPS and informed members that updates on TTURCs were requested when the project was originally approved. Dr. Croyle stated that TTURCs represent the largest collaboration effort, in terms of cofunding with the National Institute on Drug Abuse (NIDA). One of the main initiatives of the TTURCs was to include noncancer scientists, neuroscientists, pharmacologists, and policy researchers to move research from bench to bedside to public health policy. Dr. Croyle emphasized that the presentations would exemplify how TTURCs had met the goals.

Dr. Croyle introduced Dr. Scott Leischow and acknowledged Drs. Nancy Kaufman, Barbara Rimer, and Jay Turkhan for the roles they played in launching the TTURCs.

Description of TTURC Initiative. Dr. Scott Leischow, Chief, Tobacco Control Research Branch, DCCPS remarked that the percentage of current tobacco use among adolescents and adults is relatively the same as it was in the 1990s. The target goals of *Healthy People 2010* are to reduce tobacco use by adolescents from approximately 32 percent to 16 percent and by adults from approximately 23 percent to 12 percent. TTURCs were initially funded to focus research on the biological, behavioral, and social determinants of tobacco use to aid in the development of effective prevention and treatment interventions. Dr. Leischow remarked that the initiative ensures that a critical mass of investigators addresses the leading cause of cancer death, includes pilot projects to pursue new research opportunities, ensures shared resources for greater efficiency, and fosters transdisciplinary collaborations within and across centers.

Members were told that TTURCs are composed of individual research centers and have achieved a high degree of collaboration. Collaborations within TTURCs, as well as those with non-TTURC investigators, allow critical questions to be addressed that a single center could not investigate on its own. A number of collaborations currently in place were highlighted. He informed members that several focus on tobacco use in Asian versus non-Asian populations in the United States and China. The collaborations include studying the effects that economic factors, genetic polymorphisms, and mood and social settings have on the incidence of or predisposition to smoking.

Dr. Leischow noted that all of the TTURCs are collaborating on a special issue of the journal *Nicotine and Tobacco Research*, which will be published this summer. The journal will focus on transdisciplinary papers on conceptual models of tobacco initiation and use, youth smoking, transdisciplinary research infrastructure and development, training, measurements, and methods.

Vectors of Tobacco Use Vulnerability in Adolescents and Young Adults. Dr. Frances Leslie, Professor, University of California, Irvine (UCI), described the work performed at the

Center on Tobacco Use Susceptibility and Intervention (CTUSI). Dr. Leslie noted that the four main goals of the Center are to: 1) identify factors contributing to individual differences in tobacco use; 2) identify novel prevention or intervention strategies based on factors that contribute to an addictive phenotype; 3) influence national policy on tobacco use regulation; and 4) identify factors contributing to transdisciplinary success. While numerous research disciplines are represented at CTUSI, the main research focus is the identification of neural mechanisms underlying the initiation of tobacco use and the initial transition from use to dependence.

Dr. Leslie reviewed the key findings of four major projects and one pilot project. She described research from her laboratory that measured a preference for nicotine in rats during three periods of maturation. Human studies conducted by others investigated the influence of dispositional traits, such as hostility, that predict greater sensitivity to the effects of cigarette smoke and environmental cues for smoking in adolescents and young adults. Other studies undertaken at CTUSI and studies that demonstrated changes in neuronal activity in high-hostility nonsmokers exposed to nicotine before undertaking a CRT task were described.

Dr. Leslie concluded by emphasizing that 22 graduate students have been recruited into the program, along with 18 new faculty members new to tobacco research. In addition, the CTUSI collaborates with the Brain Imaging Center and with other TTURCs.

Genetic Influences on Nicotine Dependence. Dr. Caryn Lerman, Professor, Department of Psychiatry and the Annenberg School for Communication, University of Pennsylvania, stated that the scientific questions addressed by this TTURC center focus on genetic influences on tobacco use, as well as developmental differences, modifiers, and mechanisms that affect tobacco use and treatment. Dr. Lerman noted that several studies have investigated how a mutation in the CYP2B6 gene, which is associated with the metabolism of nicotine, affects abstinence rates of smokers participating in smoking cessation studies. She observed that female smokers with a CYP2B6 mutation had a lower abstinence rate when given a placebo during smoking cessation studies, while males with the same mutation were more likely to relapse when treated with bupropion, a non-nicotine aid to smoking cessation. Dr. Lerman noted that the studies suggested that bupropion

attenuates withdrawal symptoms, especially in female smokers with the CYP2B6 mutation.

In terms of how research can affect policy, Dr. Lerman acknowledged Dr. Alexandra Shields' research at Georgetown University that revealed that a majority of primary care physicians were interested in genetically testing their patients to assist with tailoring smoking treatments. However, physicians felt unprepared to do this due to concerns related to informed consent, insurance, and discrimination. Based on this information, the University of Pennsylvania TTURC has undertaken the facilitation of effective and ethical translation of new technologies to the clinic and the public by working with primary care physicians and the media.

Dr. Lerman closed by acknowledging the collaborations, the multidisciplinary seminar series, shared resources, training programs, and use of developmental funds made available through TTURC funding that would not have been available through an R01 grant.

Transdisciplinary Tobacco Use Research Centers: A New Model For Translational Research. Dr. Thomas Glynn, National Director of Science and Trends, American Cancer Society (ACS), reviewed the impact TTURCs have had on tobacco research and the justification for continued support for this funding mechanism. Dr. Glynn informed members that the scientific discoveries made during the past 3 years would not have occurred as quickly if TTURCs had not: 1) provided a platform to recruit new investigators into tobacco research; 2) involved other disciplines in tobacco research; 3) promoted collaborations among numerous TTURCs as well as with non-TTURC institutions; and 4) allowed members to focus less on immediate outcomes and more on developing laboratory-based research that could later lead to improved treatments and/or knowledge of tobacco addiction. He informed members that TTURCs are: 1) continuing the tradition of NCI support of clinical integration and delivery of new knowledge to the primary care setting; 2) actively involved in the development of a neurobiological model of nicotine dependence and front-line genetic and tobacco information for health care providers; and 3) helping investigators compete for funding from other external granting agencies. In closing, he noted that the TTURCs would provide information that could be used to reduce the burden of tobacco use.

In discussion, the following points were made:

- Considering the promising results from TTURC investigators, the transdisciplinary mechanism should be used to study obesity, diet, and physical activity, as well as health behaviors that can modify cancer risk within the population.

- A greater involvement of epidemiologists would add another dimension to the research conducted by TTURCs.

- Focusing on the neural mechanisms specific to the period of adolescence will aid in determining when teenagers are most susceptible to nicotine.

- The lung cancer SPOREs and TTURCs should be encouraged to collaborate to assess nicotine susceptibility in parallel with lung cancer susceptibility.

- An effort should be made to include other partners, similar to ACS, that could invest financially and provide other contributions to TTURCs.

top

X. DIVISION OF CANCER CONTROL AND POPULATION SCIENCES: PROGRAM STATUS REPORTS

Introduction . Dr. Croyle explained that one of the responsibilities of the DCCPS is to respond to the public, including Congress and advocacy groups, about public health policy issues.

Dr. Croyle introduced Drs. Deborah Winn, Eric (Rocky) Feuer, and Joseph Lipscomb.

Update of Studies of Breast Cancer on Long Island. Dr. Deborah Winn, Acting Branch Chief, Clinical and Genetic Epidemiology Research, Epidemiology and Genetics Research Program (EGRP), DCCPS, described studies that investigated the

effect of environmental risk factors contributing to the dramatically high incidence of breast cancer in two counties on Long Island, New York. Dr. Winn noted that the studies began after a bill was passed in 1993 to conduct a case-control study to assess the high incidence of breast cancer in the two counties on Long Island, another county in New York, and one county in Connecticut. A second law mandated investigating the geographical system surrounding these counties to evaluate what effect contaminated drinking water, air pollution, pesticides, and/or other factors might have had on the incidence of breast cancer.

The Long Island Breast Cancer Study Project (LIBCSP) comprised ten individual studies. Dr. Winn presented one study that investigated an association between organochlorines, including pesticides, and polycyclic aromatic hydrocarbons (PAHs) from incomplete combustion and the incidence of breast cancer on Long Island. She noted that residents of Long Island as well as advocacy groups were involved and continue to be involved in the study.

Members were told that the Long Island geographic information system (GIS) integrates environmental and breast cancer databases with mapping capabilities as well as provides a statistical tool for analysis. The Web site allows the research community to investigate potential exposures to numerous chemicals in a specific region within a county.

Dr. Winn commented on studies investigating the potential breast cancer cluster in Marin County, California. In closing, she noted that several groups are working together to create a GIS for Marin County.

Cancer Intervention and Surveillance Modeling Network (CISNET). Dr. Eric Feuer, Statistical Research and Applications Branch, Surveillance Research Program (SRP), DCCPS, presented an overview of studies completed, in progress, and planned by the CISNET consortium on breast, prostate, and colorectal cancer. CISNET's goal is to model the impact of cancer control interventions, such as screenings, treatments, and preventive measures, on current and future cancer trends. Since 2000, 17 grantees have been funded for 4 years through U01 Cooperative Agreements. The grantees represent a diverse group of cancer modelers in the United States and the Netherlands.

Dr. Feuer described the CISNET breast cancer "base case" that investigated the impact of mammography, adjuvant therapy, and the combination of both on U.S. breast cancer mortality from 1975 to 2000. He noted that the breast cancer mortality rate has dropped since 1990, mainly due to increased mammography screening combined with the use of multiagent chemotherapy and tamoxifen. Members were told that a second breast cancer base case study modeled the consequences of underinsurance or lack of insurance on cancer screening, treatment, and mortality. The results will be included in the last in a series of six reports, Strategies and Models for Providing Health Insurance, due in late summer 2003.

Two prostate cancer-modeling studies were presented. The first study used recent incidence trends to estimate the extent of overdiagnosis of prostate cancer as a result of prostate-specific antigen (PSA) screening. The second study involved simulating ecologic studies of the effectiveness of PSA screening by comparing the mortality rate between areas of high and low PSA screening. Colorectal cancer modeling studies were also presented.

The last study presented was the Healthy People 2010 Midcourse Correction Review; DHHS's blueprint for achieving the nation's health goals of increased quality of life and elimination of health disparities. CISNET modeling will determine if 2010 goals for treatment, screening, and prevention will meet the 2010 mortality goals.

In discussion, the following points were made:

- The PSA prostate study should include dissemination of different treatments and link that to screening in relation to the relative impact of treatment and screening on mortality. The treatments should also include variations in quality of care across the country.

- Statisticians and graduate students should be recruited into the modeling studies.

Improving the Quality of Cancer Care. Dr. Joseph Lipscomb, Chief, Outcomes Research Branch, DCCPS, NCI, provided an overview of the Quality of Care (QOC) Initiative, which began after reports from several groups determined that there were wide

variations in who received and what constituted quality cancer care. The Initiative's goals were to improve quality of care for cancer patients by strengthening the scientific basis for public and private decision making on care, coverage, purchasing, regulations, and standard-setting. Dr. Lipscomb reviewed a number of NCI-sponsored research activities funded independently of the Initiative, but with the same goals and objectives. He presented examples of results obtained over the previous 15 years from 40 POC/QOC studies. Dr. Lipscomb commented that investigators and members of the public are aware of the quality of care studies and the demand for the data has increased.

Three current QOC initiatives presented were the: 1) Cancer Outcomes Measurement Working Group (COMWG) whose goals are to evaluate the state of the science in outcomes measurement and recommend approaches for improving the state of the science. Findings will be published in a book entitled *"Outcomes Assessment in Cancer"*; 2) Quality of Cancer Care Committee (QCCC) which is a collaborative effort among the Federal agencies that deliver, pay for, regulate, or perform research on cancer care; and 3) Cancer Care Quality Measures Project (CanQual) created as a public-private collaboration to identify a core set of measures for improving the quality of cancer care.

Dr. Lipscomb remarked that a second phase has just begun that would entail the creation of a technical expert panel for each of the areas identified in the first phase. An evidence-based review panel would be associated with each technical panel, and the panels would submit recommendations to a main steering committee. The long-term goal is that the recommendations will become the Voluntary Consensus Standards used to guide Federal and private agencies in making quality-of-care decisions.

In discussion, the following points were made:

- The QOC should promote research to understand why cancer care declines as people age. One way to accomplish this is by initiating RFAs specific to such research.

- Clinicians should be included in studying the disparities in cancer care of older patients and between patients with different categories of the same type of cancer.

- Funding for investigator-initiated research to address quality-of-care interventions should be provided in parallel to these efforts.

Adjournment: The meeting adjourned at 12:10 p.m. on Tuesday, 4 March 2003.

top