

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
6TH JOINT MEETING OF THE BOARD OF SCIENTIFIC ADVISORS
AND THE NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
December 1, 2015**

**Building 31C, Conference Room 10
National Institutes of Health
Bethesda, Maryland**

**BOARD OF SCIENTIFIC ADVISORS and
NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
December 1, 2015**

The Board of Scientific Advisors (BSA) and the National Cancer Advisory Board (NCAB) convened for the 6th Joint Meeting on 1 December 2015, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, 1 December 2015, from 8:30 a.m. to 2:38 p.m., and closed to the public from 2:39 p.m. to 4:00 p.m. The NCAB Chair, Tyler E. Jacks, Director, Koch Institute for Integrative Cancer Research, David H. Koch Professor of Biology, Massachusetts Institute of Technology, and the BSA Chair, Dr. Chi V. Dang, Director, Abraham Cancer Center, Professor of Medicine, Perelman School of Medicine, University of Pennsylvania, presided during the open session. Dr. Jacks presided during the closed session.

BSA Members

Dr. Chi V. Dang (Chair)
Dr. Francis Ali-Osman
Dr. Kenneth C. Anderson
Dr. Dafna Bar-Sagi
Dr. Ethan M. Basch
Dr. Sangeeta N. Bhatia (absent)
Dr. Andrea Califano (absent)
Dr. Arul M. Chinnaiyan
Dr. Graham A. Colditz
Dr. Joseph M. DeSimone (absent)
Dr. Daniel C. DiMaio
Dr. Brian J. Druker
Dr. Karen M. Emmons
Dr. Carol E. Ferrans*
Dr. Stanton L. Gerson
Dr. Joe W. Gray
Dr. Chanita Hughes-Halbert (absent)
Dr. James V. Lacey*
Dr. Theodore S. Lawrence
Dr. Maria E. Martinez (absent)
Dr. Luis F. Parada (absent)
Ms. Diane Zipursky Quale
Dr. Martine F. Roussel
Dr. Victoria L. Seewaldt*
Dr. Kevin M. Shannon
Ms. Mary L. Smith
Dr. Lincoln D. Stein (absent)
Dr. Gregory L. Verdine (absent)
Dr. Cheryl L. Walker
Dr. Eileen P. White
Dr. Kevin P. White

* pending appointment

NCAB Members

Dr. Tyler E. Jacks (Chair)
Dr. Peter C. Adamson
Dr. Deborah Watkins Bruner
Dr. Yuan Chang
Dr. David C. Christiani
Dr. Marcia R. Cruz-Correa (absent)
Dr. Kevin J. Cullen
Dr. Judy E. Garber (absent)
Dr. Elizabeth M. Jaffee
Dr. Beth Y. Karlan
Dr. Timothy J. Ley
Dr. Olufunmilayo F. Olopade
Dr. Mack Roach, III
Dr. Jonathan M. Samet
Dr. Charles L. Sawyers
Dr. William R. Sellers (absent)
Dr. Max S. Wicha

Alternate Ex Officio NCAB Members

Dr. Robert T. Anderson, DOE (absent)
Dr. Michael A. Babich, CPSC (absent)
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS
Dr. Richard Pazdur, FDA (absent)
Dr. Craig D. Shriver, DOD (absent)
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH (absent)
Dr. Richard J. Thomas, OSHA/DOL

President's Cancer Panel

Dr. Barbara K. Rimer (Chair) (absent)
Mr. Hill Harper (absent)
Dr. Owen Witte (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Douglas R. Lowy, Acting Director, National Cancer Institute
Dr. Jeff Abrams, Director, Division of Cancer Treatment and Diagnosis
Dr. Lynn Austin, Executive Officer, Deputy Director for Management
Dr. L. Michelle Bennett, Director, Center for Research Strategy
Dr. Stephen J. Chanock, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Acting Director, Office of Cancer Centers
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. James Doroshow, Deputy Director for Clinical and Translational Research
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Peter Greenwald, Associate Director for Prevention
Dr. Ed Harlow, Special Advisor to the Acting Director
Dr. Toby Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Lee Helman, Acting Director, Center for Cancer Research
Dr. Warren Kibbe, Director, Center for Bioinformatics and Information Technology
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Jerry Lee, Director, Center for Strategic Scientific Initiatives
Dr. Glenn Merlino, Acting Scientific Director for Basic Research, Center for Cancer Research
Dr. Craig Reynolds, Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Dinah Singer, Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis Staudt, Director, Center for Cancer Genomics
Dr. Ted Trimble, Director, Center for Global Health
Mr. Michael Weingarten, Director, Small Business Innovation Research
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Robert Wiltrot, Special Advisor to the Acting Director
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Carolyn Aldige, Cancer Research and Prevention Foundation
Dr. Carolyn Best, American Urological Association
Ms. Paula Bowen, Kidney Cancer Association
Dr. Susan Braun, National Cancer Institute, Council of Research Advocates
Mr. William Bro, Kidney Cancer Association
Dr. Carol Brown, Society of Gynecologic Oncologists
Mr. Matthew Farber, Association of Community Cancer Centers
Dr. Margaret Foti, American Association for Cancer Research
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Ms. Shandi E. Hill, American Society of Therapeutic Radiology and Oncology
Ms. Ruth Hoffman, Candlelighters Childhood Cancer Foundation
Dr. Gerald F. Joseph, Jr., American College of Obstetricians and Gynecologists
Ms. Rebecca A. Kirch, American Cancer Society
Dr. Steven Klein, National Science Foundation
Ms. Laura Levit, American Society of Clinical Oncology
Dr. W. Marston Linehan, Society of Urologic Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education

Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Johannes Vieweg, American Urological Association
Ms. Pamela A. Wilcox, American College of Radiology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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TUESDAY, DECEMBER 1, 2015

I. CALL TO ORDER AND OPENING REMARKS—DRS. CHI V. DANG AND TYLER E. JACKS

Dr. Jacks called to order the 6th Joint BSA and NCAB meeting and welcomed members of the Board, *ex officio* members of the Board, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Drs. Chi and Jacks reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Dr. Jacks welcomed the new BSA members: Drs. Carol Ferrans, Professor and Associate Dean for Research, Director, UIC Center of Excellence in Eliminating Health Disparities, Department of Biobehavioral Health Sciences, College of Nursing, University of Illinois at Chicago; James Lacey, Jr., Associate Professor, Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute; and Victoria Seewaldt, Ruth Ziegler Professor, Chair, Department of Population Sciences, Beckman Research Institute, City of Hope.

Motion. A motion to approve the minutes of the 16 September 2015 NCAB meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DRS. CHI V. DANG AND TYLER E. JACKS

Dr. Jacks called Board members' attention to future meeting dates.

III. NCI ACTING DIRECTOR'S REPORT—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Acting Director, welcomed members of both the NCAB and BSA to the sixth joint meeting of these Boards and recognized the new members. Dr. Lowy reviewed the agenda and provided an update on the NCI budget and several activities.

Fiscal Year (FY) 2015 Research Project Grant (RPG) Success Rates. Dr. Lowy referred members to the NCI's website for newly released data about the research project grant (RPG) success rates, and he described shifts in the rates for R01 and R21 applications since FY 2012, with success rates of 14 percent for R01 applications and 12 percent for R21 applications in FY 2015. The first Outstanding Investigator Awards (OIAs) also were made in FY 2015, which will put pressure on the funding pool, but the NCI hopes to maintain the R01 and R21 award levels. Dr. Lowy said that sequestration reduced the NCI's budget in FY 2013 and resulted in a modest reduction in the competing RPGs from FY 2012 to FY 2013. Approximately \$50 million (M) was added to the RPG pool in each of FY 2014 and FY 2015, when the NCI's budget increased by \$140M and \$21M, respectively. Members were reminded that the NCI continues to operate on a Continuing Resolution (CR).

Research Specialist Award (RSA). Dr. Lowy stated that the new RSA (R50) has been approved with applications due in February 2016. The potentially renewable 5-year award will support a new career path with stable salary support for accomplished scientists who want to continue to do research but who do not want to be a principal investigator (PI). The RSA will support that portion of salary dedicated to NCI-funded cancer research and will include travel funds of up to \$5,000 per year, but it will not cover research expenses. The application requires a letter from the sponsoring PI, and the research specialists would have the independence to move to another laboratory or institution with prior approval from the NCI.

New Cryo-Electron Microscopy (cryo-EM) User Facility at the Frederick National Laboratory for Cancer Research (FNLCR). Members were informed that a new cryo-EM user facility at the FNLCR will provide the extramural research community access to high-quality cryo-EM. The development of high-quality images will help to determine structures of macromolecules of importance in cancer research. Dr. Lowy told members that the Frederick National Laboratory Advisory Committee (FNLAC) recommended the establishment of the facility at its meeting in September 2015. Dr. Sriram Subramaniam, Center for Cancer Research (CCR), will serve as the facility's Director, with oversight provided by a steering committee composed of members of the FNLAC and the cryo-EM and structural biology communities. The FNLAC agreed with a modest user fee to ensure commitment on the part of the laboratory using the facility. The Titan KRONOS will anchor the facility, allowing researchers to potentially determine high resolution without three-dimensional crystals, structural analysis of dynamic protein assemblies, and progressively higher resolution. Cryo-EM and related technologies have sharpened cellular imaging resolution from 9 to 2.2 angstroms during the past 15 years, which has provided an ideal opportunity to better support and advance cancer research.

NCI Workshop on Cancer Health Disparities. Dr. Lowy reported on a cancer health disparities workshop held in November 2015 to help develop research priorities for the NCI in cancer health disparities. Co-Chairs included Drs. Lisa Richardson, Centers for Disease Control and Prevention (CDC); Edith Mitchell, Thomas Jefferson University; Sandy Markowitz, Case Western Reserve University; and Michelle Bennett, NCI. The workshop considered the elevated risks in high-risk, minority populations for breast, prostate, colorectal, liver, and multiple myeloma cancers based on biology, lifestyle, access to and utilization of care, and short-, intermediate-, and long-term activities that could mitigate the risks. Workshop participants recommended several research priorities, including the study of a cohort focused on minority individuals who develop cancer at an unusually early age, and the issue of financial toxicity, which can affect the implementation of cancer care for minority populations.

Dr. Lowy reflected on the workshop discussions on colorectal cancer, a disease that has increased in incidence and mortality among African Americans. Two ideas that the workshop participants identified to help reduce disparities in colorectal cancer were the best algorithms to follow for screening and follow-up, and the effectiveness of prevention through chemoprevention and lifestyle factors. Collaborations with other organizations, such as the Patient-Centered Outcome Research Institute (PCORI), can accelerate such research, and NCI leadership has been discussing the potential collaborative activities with Dr. Joe Selby, PCORI Director. The NCI and National Heart, Lung, and Blood Institute (NHLBI) also are discussing a possible joint project to promote the use of aspirin to prevent both cardiovascular disease and colorectal cancer following the United States Prevention Services Task Force's (USPSTF) recommendations for aspirin use for these purposes. Dr. Lowy noted that aspirin uptake for reducing the risk of cardiovascular disease is lower among African Americans. He encouraged members to read and share their ideas on an NCI blog highlighting health disparity efforts in biology, clinical trials, and the training of a more diverse workforce (www.cancer.gov/cancer-currents).

New Pilot Project With Department of Energy. Dr. Lowy described a partnership with the Department of Energy (DOE) to advance cancer research and high-performance computing in the United States. The DOE's expertise with computing, data analysis, and experiment-driven co-design of extreme scale simulation in data-driven analysis will assist the NCI in its precision oncology research and clinical applications. A proposed pilot project will use predictive models for preclinical screening with the goal of improving those predictions about the biology of tumors and responses to various treatments.

NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) Trial. Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, provided an update on the NCI-MATCH trial, which was initiated in August 2015 under the leadership of the ECOG-ACRIN Cooperative Group and an NCI team. The trial involved a national effort that accrued more than 500 patients in approximately 9

weeks. Dr. Doroshow stated that the trial has reached a phase for a planned “pause” in patient accrual during which the characteristics of the initially accrued patient population are being reviewed, including allowing the NCI to ensure that rare cancers comprise 25 percent of those accrued. Members also were told that work is underway with the Central Institutional Review Board (CIRB) to open as many as 7-10 additional drug treatment arms in time for the next phase of accrual, and two more laboratories are being sought to help with sequencing activities.

Questions and Answers

Dr. Cheryl L. Walker, Professor and Director, Institute of Biosciences and Technology, Center for Translational Cancer Research, Welch Chair in Chemistry, Texas A&M Health Science Center, asked about the shift in funding levels over time for modular and larger grants. Dr. Lowy referred to his previous presentation to the Joint Boards in 2014 and said that the NCI reduced the expected cut to modular grants from 17 to 8.5 percent following that presentation and the Joint Boards’ input.

Dr. Kevin M. Shannon, Roma and Marvin Auerback Distinguished Professor in Molecular Oncology, American Cancer Society Research Professor, Department of Pediatrics, University of California, San Francisco, wondered about the aggressive 3-year timeline to determine the predictive qualities of the preclinical model through the pilot project with the DOE. He also asked how the project might address issues regarding clonal heterogeneity. Dr. Doroshow agreed that the timeline presents challenges but noted that a considerable amount of therapeutic and sequenced data from a number of NCI models will be provided to the DOE. Dr. Shannon observed that patient-derived xenograft (PDX) models and cell line models do not recapitulate clonal heterogeneity, even though a large proportion of drug resistance and relapse is due to inherent genetic instability and clonal heterogeneity. Dr. Doroshow responded that models in individual subjects from whom biopsies are taken at fast autopsies may provide answers.

In response to a query by Dr. Kevin P. White, James and Karen Frank Family Professor, Department of Human Genetics, Professor, Department of Ecology and Evolution, and Director, Institute for Genomics and Systems Biology, Knapp Center for Biomedical Discovery, The University of Chicago, about the resources needed to sequence data from the NCI-MATCH trial, and suggestion to provide the extramural community with quicker access to the data, Dr. Doroshow stated that the NCI worked extensively to determine the additional resources needed for sequencing sites and developed substantial contingency plans to ensure that the sites would handle the expected high volume of data expeditiously. Dr. Barbara Conley, Associate Director, Cancer Diagnosis Program (CDP), Division of Cancer Treatment and Diagnosis (DCTD), confirmed that dissemination of data will be shared after each arm is finished and will not wait until the end of the entire accrual phase for the study. Dr. Warren Kibbe, Director, Center for Biomedical Informatics and Information Technology (CBIIT), added that data will be made available through the Genomic Data Commons.

Dr. Joe W. Gray, Gordon Moore Endowed Chair, Department of Biomedical Engineering, Director, OHSU Center for Spatial Systems Biomedicine, and Associate Director for Biophysical Oncology, Knight Cancer Institute, Oregon Health and Science University, asked about the DOE’s role in the proposed pilot program. Dr. Kibbe indicated that the activity is an intellectual and resource partnership and that DOE scientists would be involved. Dr. Lowy confirmed the DOE’s considerable interest and added that he and Dr. Kibbe met with Dr. Ernest Moniz, DOE Secretary, at his request about the partnership.

In response to a request for clarification by Dr. Jacks, NCI staff confirmed that the RSA would be used to offset the research specialist’s salary that is paid under NCI-funded cancer research and would not comprise additional monies to the PI.

Dr. Mack Roach III, Professor of Radiation Oncology and Urology, Director, Particle Therapy Research Program & Outreach, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, lauded the NCI on its FY 2017 Bypass Budget Report, which describes the NCI's investment in research.

IV. PRESIDENT'S CANCER PANEL REPORT—DR. ABBY B. SANDLER

Dr. Abby B. Sandler, Executive Secretary, President's Cancer Panel (the Panel), Office of the Director, and Special Assistant to the Director, Rare Tumors Initiative, CCR, provided an update on the activities of the Panel, which has as its mission to monitor the development and execution of the National Cancer Program and report directly to President concerning any delays or blockages in the rapid execution of the Program. Dr. Sandler reminded those present that members of the Panel include Dr. Barbara K. Rimer, University of North Carolina at Chapel Hill (Panel Chair); Mr. Hill Harper, cancer survivor, actor, and author; and Dr. Owen N. Witte, University of California, Los Angeles.

Members were informed that the report on the 2012–2013 Panel series titled “Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer,” which was released in early 2014, continues to have influence, with such responses as a Request for Proposals released by the National HPV Roundtable (a coalition of public, private, and voluntary organizations to increase HPV vaccination coverage) and a keynote presentation on the report at the Cancer Prevention Research Institute of Texas' Innovations in Cancer Prevention and Research Conference. The NCI's research on the topic includes a proposed trial on single-dose treatment that is responsive to the Panel's recommendation to safely reduce the number of doses, as well as Cancer Center grant supplements to gather local data on vaccine uptake, barriers, needs, and collaborators.

Dr. Sandler reminded members that the 2014–2015 Panel series on “Connected Health: Improving Patients' Engagement and Activation for Cancer-Related Health Outcomes” included a planning meeting and three workshops co-chaired by Drs. David K. Ahern and Bradford W. Hesse, Division of Cancer Control and Population Sciences (DCCPS), and attended by experts in the field of connected health, as well as a number of patient advocates; the Panel will publish its report on the topic in 2016. The third workshop held in July 2015 explored cancer as a charismatic species for health care; the need for a uniform, open-source interface regarding electronic health records (EHRs); stakeholder collaboration; patient engagement; broadband access to rural and underserved areas; and patient-reported outcomes for clinical care and research. Twitter chats organized by the patient advocates provided additional input to the workshops from the cancer patient community regarding how connected health could help meet critical health care needs among patients and families, increase patient activation, and identify communication tools to better engage patients. The connected health scenario envisioned by the Panel involves four areas: (1) personal health information and data sharing (e.g., EHR interoperability and access to data); (2) person- and family-centered care; (3) devices, sensors, and apps; and (4) a national health information infrastructure. The Panel has met with stakeholders, including the U.S. Department of Health and Human Services (HHS) Office of the National Coordinator for Health Information Technology and the Federal Communications Commission, and meetings are planned with additional organizations, such as the American Society of Clinical Oncology (ASCO).

Dr. Sandler stated that the Panel is planning the 2016 series, which will address the topic of the rising costs of and access to cancer care. High drug prices in the news have raised public awareness about this issue, and the costs of cancer care are unsustainable. Cancer care is one of the fastest growing sectors of health care costs, and the cost in the United States was an estimated \$125 billion (B) in 2010. During the past 15 years, the average price of new cancer drugs increased five- to 10-fold, and in 2014 all new cancer drugs approved by the U.S. Food and Drug Administration (FDA) were priced above \$120,000 per

year of use. The Panel will hold a planning workshop in the spring of 2016 to discuss these issues and frame a series to explore potential solutions to the rising costs of cancer care.

Questions and Answers

Dr. Peter C. Adamson, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital in Philadelphia, queried about the process to select topics. Dr. Sandler responded that the criteria for selection included that topics be timely, that they involve a problem facing the National Cancer Program, and that they result in a report that will have influence in the cancer community and have actionable recommendations.

Dr. Olufunmilayo F. Olopade, Walter L. Palmer Distinguished Service Professor of Medicine and Human Genetics, Associate Dean for Global Health, and Director, Center for Clinical Cancer Genetics, The University of Chicago, Pritzker School of Medicine, encouraged efforts to integrate the patient community with the data and genomic science communities. Dr. Sandler agreed but noted challenges with the validation of data from devices, sensors, and apps. She mentioned Dr. Witte's perspective that the genetic data, treatment options, and other information about patients' tumors should be included in their EHRs. Dr. Jacks encouraged the Panel to include representatives from industry throughout the process as they carry out the upcoming series on rising costs of cancer care.

Dr. Ethan M. Basch, Associate Professor of Medicine, Division of Hematology/Oncology, and Director, Cancer Outcomes Research Program, University of North Carolina at Chapel Hill, asked about the engagement of partners to move the process forward once recommendations have been made. Dr. Sandler said that for the HPV report, the stakeholders who would be needed to implement recommendations were involved throughout the discussions even as the recommendation language was crafted. Dr. Robert Croyle, Director, DCCPS, stated that as a result of that engagement and the need for a visible leadership role in local communities' supporting HPV vaccination uptake, a consortium including NCI Cancer Centers and the CDC has been established to engage different sectors in the uptake issues at the local level.

V. LEGISLATIVE REPORT—MS. M. K. HOLOHAN

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations, reported on appropriations, Congressional hearings, and legislation of interest. Ms. Holohan stated that the 21st Century Cures Act passed in the House, and a parallel bill is being developed in the Senate. Members were informed that the House and Senate Committees approved their FY 2016 appropriations bills in June 2015, both including \$200M for the Precision Medicine Initiative, of which \$70M is for oncology. The House bill allocated to the NIH and NCI \$31.2B and \$5.081B, respectively. The Senate bill provided to the NIH and NCI \$32B and \$5.204B, respectively. Dr. Lowy attended two NIH appropriations hearings in the Senate, the first in April and the second in October 2015.

Ms. Holohan reviewed changes in Congressional leadership and noted that the NCI continues to work under a continuing resolution (CR) through December 11, 2015. President Barack Obama signed the Bipartisan Budget Act of 2015 into law on November 2, which suspends the U.S. debt limit until March 2017, partially rolls back the sequester, and increases discretionary spending caps for FY 2016 and 2017. Ms. Holohan reflected on the potential impact of a bill about Syrian refugees on NIH appropriations and an FY 2016 funding increase for the NCI, noting that refugee issues will need to be incorporated into the \$1.1 trillion omnibus spending bill, as well as expected controversial policy riders and partisan disagreements that may affect the passage of an appropriations bill.

VI. CANCER CENTERS WORKING GROUP REPORT—DRS. CHI V. DANG AND STANTON L. GERSON

Drs. Chi V. Dang and Stanton L. Gerson, Shiverick Professor of Hematological Oncology, Director, Case Comprehensive Cancer Center, Director, National Center for Regenerative Medicine, Case Western Reserve University, and Director, Seidman Cancer Center, University Hospitals Case Medical Center, provided a report of the Cancer Centers Working Group. Dr. Dang reminded members that the 69 NCI-designated Cancer Centers conduct the majority of NCI extramurally funded research, provide a critical platform for NCI's clinical trials effort and the Precision Medicine Initiative (PMI), and promote collaborations and team science. The Cancer Centers Working Group provided recommendations to the NCI in February 2014 to address funding imbalances experienced by some Centers. The NCI began testing several models, but was faced with the difficulty that with each formula some Centers would suffer drastic decreases in funding. The Working Group expressed concerns about implementing a formula that reduces some awards because of the infrastructure supported by the NCI and institutional commitment by academic entities. A rebalance of Cancer Center Support Grant (CCSG) funding to distribute any new money in the program to the most meritorious and underfunded Centers would allow every Center the opportunity to increase its award during the rebalancing period.

The Working Group recommended three rebalancing phases for CCSG funding. Phase 1 would establish base awards by type of Center and bring all Centers up to the new base in FY 2016, as recommended by the NCAB, with direct benefits to approximately one-half of the Centers. Phase 2 (FY 2017–2021) would allocate new CCSG funds using the NCAB-recommended metrics of the size of the cancer-relevant research base of a Center and the merit achieved in the review of its next competitive application. In Phase 3, which is proposed for FY 2022, the NCI would reconsider further rebalancing, continue the effort with more new money, and/or adopt a zero-based formula as recommended by the NCAB. Additional funding beyond Phase 2 could be added following a sustained increase in the NCI budget.

Members were told that the Working Group differentiated between NCI, NIH, and non-NIH funding sources and considered ratios to determine the maximum budget eligibility for Centers based on these sources. Advantages to all NIH cancer-relevant funding include that cancer-relevant funding from other NIH Institutes is important to the Cancer Centers, a uniform reporting date could be implemented, and an NIH database could be used to distinguish cancer-relevant funding. However, the database would not indicate how much of the NIH grant is cancer relevant, and the NCI does not have the resources to examine each grant in the Cancer Centers to determine the percentage of cancer relevance. Regarding other peer-review funding sources, cancer-relevant funding from other Federal, state, and private sources is important to the Cancer Centers and comprised 17 percent of all funding reported by the Centers in FY 2014. However, the NCI is unable to verify these sources to confirm grants, funding levels, cancer relevance, or active dates, and many of these funding sources are limited to Centers within a state. The Centers overall would not experience a difference with NCI-only versus NIH cancer-relevant funding. The Working Group recommended that the increment to which Centers could apply for a funding increase be adjusted up to that curvilinear max based on a merit score, reintroducing the value of the review and the merit score in the funding alignment.

Dr. Gerson stated that the Working Group's conclusions were to fully support implementation of Phase 1, incorporate Phase 2 into the CCSG funding plan contingent on NCI funding and use of total cancer-related NIH funding to define the benchmark funding curve with the sliding scale proposed, and encourage ongoing attention to Phase 3 and beyond and giving consideration to other issues of importance to the Cancer Centers, including supplement awards.

Questions and Answers

Dr. Walker asked about the small differential in baseline numbers between the clinical and comprehensive Cancer Centers. Dr. Gerson replied that the baseline numbers were an element of the NCAB's original report. Dr. Lowy agreed that a larger differential could exist in a different funding environment, noting that the model reflects a compromise that fits within the current projected NCI budget.

Members strongly encouraged the NCI to refine the review process for the proposed Phase 2 funding model to accommodate funding received by Cancer Centers from other agencies. Dr. Basch noted that a significant amount of support for the conduct of population science is provided by other organizations, such as PCORI. Drs. Jacks and Shannon agreed on the need to incorporate non-NIH/non-NCI funding sources as part of the review process. Dr. Brian J. Druker, Director, OHSU Knight Cancer Institute, Associate Dean for Oncology, OHSU School of Medicine, and JELD-WEN Chair of Leukemia Research, OHSU, encouraged the review process, particularly the site visit, to remain focused on the cancer science.

Dr. Max S. Wicha, Deputy Director of the Taubman Institute, Distinguished Professor of Oncology, and Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan, reflected on the importance of the NCI designation, which provides a great benefit to the clinical enterprise for clinical and comprehensive Cancer Centers, and he encouraged the NCI to accelerate the schedule proposed for the funding readjustment.

In response to concerns expressed by Dr. Theodore S. Lawrence, Isadore Lampe Professor and Chair, Department of Radiation Oncology, University of Michigan Medical School, about bias against smaller centers, Dr. Paulette Gray clarified that no discussion of the size of the Center occurs during the review process, which is based on the application that is submitted and the quality of the presentations at the site visit. Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenebaum Cancer Center, and Professor of Medicine, University of Maryland, wondered whether a formula that permits increases based on merit would disadvantage smaller Centers from receiving future funding increases. Dr. Lowy affirmed the NCI's approach that Centers that perform well should have the potential to receive an increase, irrespective of a Center's size, and he cautioned that the potential for funding increases varies with the size of the NCI budget. Dr. Dang clarified that the merit score model is based on historical data.

Motion. A motion to accept the report of the BSA Cancer Centers Working Group Report was approved unanimously, with the stipulations that the NCI leadership (1) review what non-NCI funding sources, both NIH and non-NIH, should be considered in the funding base for all Cancer Centers; (2) develop a simple and transparent process for evaluating the cancer relevance of non-NCI funding from these other sources; (3) when performing the evaluation, consider the potential impact on outlier institutions that would benefit from or be hurt by any new formula for considering non-NCI funding; and (4) present the NCI's response to these areas, as well as how to use merit scores and careful modeling, at the next BSA meeting.

VII. SEER REGISTRIES: ENHANCING THE MISSION TO SUPPORT CANCER RESEARCH—DRS. ROBERT CROYLE AND LYNNE PENBERTHY

Drs. Robert Croyle, Director, DCCPS, and Lynne Penberthy, Associate Director, Surveillance Research Program, DCCPS, presented new strategies to re-envision the role of Surveillance, Epidemiology, and End Results (SEER) registries. Dr. Penberthy provided an overview of the SEER Program and reminded members that SEER population-based registries cover 30 percent of the U.S. population and integrate more than 400,000 incident cases reported annually, SEER data are most

commonly used to represent trends over time, and SEER is the only population-based system in the United States that includes a broad set of clinical variables. To ensure data completeness and rigorous quality control, real-time electronic pathology report feeds are being expanded in more than 360 laboratories, including intensive visual editing of key data at the central registry level for accuracy across multiple reporting sources and optimizing methods to ensure complete and accurate data through re-abstraction and focused review. Members were told that SEER registries are located at or associated with NCI-designated Cancer Centers, facilitating integration between SEER PIs and Centers. Dr. Penberthy stated that cancer surveillance challenges involve data collection and encompass the complexity of cancer care, the need to expand data characterizing each cancer, and the current manual processes for abstraction and data capture. Data sources include the dispersion of cancer diagnosis and treatment across multiple health care providers/locations as well as hospitals, which require accessing information outside of traditional registration sources (e.g., pathology laboratories, physician offices, pharmacies, and freestanding integrated specialty practices). Dr. Penberthy next outlined four strategic priorities for the SEER Program and described potential concepts for each.

(1) **Represent data in more clinically relevant categories.** Because statistics by organ site do not represent cancer as it is currently understood and treated, statistics could be presented by clinically relevant categories, such as histology or molecular characterization. For example, esophageal cancer in men could be presented overall and by histologic subtype, or breast cancer incidence could be reported by subtype and race/ethnicity.

(2) **Automate and directly capture data via linkages and auto-processing of data.** To counter the lack of complete and detailed treatment, linkages could be made with existing data for pharmacy-provided oral drugs, or standardized claims for infusion therapy could be captured and processed. Members were informed that there is no population-based information on oral agents, and capturing pharmacy data offers the potential for supplementing treatments, monitoring disparities in use and nonadherence, and identifying adverse events. A pilot study is underway linking with IMSHealth, which covers 70 percent of pharmacy transactions, with four SEER registries to compare completeness with Medicare Part D patterns of care and some special studies for breast cancer, colon, chronic myelogenous leukemia, and multiple myeloma; a preliminary analysis shows that in the SEER data, about 45 percent of women older than 65 with breast cancer currently are reported to have received hormonal therapy, whereas adding Medicare Part D and IMS Health data shows that approximately 72 percent of women actually are receiving hormonal therapy. Additional linkages could include large pharmacy chain central repositories, pharmacy processors or “switchers,” and claims data for infusion therapy. Dr. Penberthy shared preliminary data from an ongoing pilot study of Georgia oncology practices to demonstrate the level of data on the treatment of initial and recurrent breast cancer available in 6 months of claims from four oncology practices.

In addition, the capture of clinical data could be completed through automation and directly via linkages. To address the inability of registries to access relevant clinical test results, partnerships could be established with commercial entities that perform tests for direct data feed. Examples of linkages with such commercial partners as Oncotype DX were shared that demonstrated a notable increase (40%) in test results that could be added to existing data from hospital-reported results.

(3) **Automate and directly capture data via auto-processing and natural language processing.** Data capture is challenged by the fact that key data are stored in the form of unstructured text. This could be resolved by leveraging existing capacity across academic and commercial enterprises for natural language processing and data extraction. Specific approaches could be to focus on unstructured electronic pathology reports, expand data not collected or available only in unstructured text, and leverage lessons learned to other unstructured text, such as radiologic imaging dictations.

(4) **Expand outcomes data collection.** Because survival is no longer the only important outcome for cancer patients, multiple data sources should be leveraged for disease status and patients should be engaged in the process. Dr. Penberthy proposed a SEER-linked virtual biorepository that would be population based; be available across a broad spectrum of health care facilities and pathology laboratories; and provide access to rare cancers, exceptional outcomes, linked long-term outcomes, and existing annotation with clinical and demographic data with the potential for custom annotation. The biorepository would be renewable, with more than 400,000 incident cases added annually. Members were told that a pilot repository project on pancreatic and breast cancer is underway with seven registries to assess best practices across multiple registries, estimate the costs of supporting a SEER-wide system, and assess the availability of specimens.

Dr. Penberthy described a virtual pooled registry with the North American Association of Central Cancer Registries (NAACCR) and National Program of Cancer Registries (NPCR), which would serve as a virtual national cancer registry and provide a tool for researchers to automatically link patients with all U.S. cancer registries. Its aims would be to automate linkages, operate under a centralized institutional review board (IRB), and facilitate the return of patient information on cancers, survival, cause of death, treatment, and other information. The NCI would benefit from a virtual registry with potential cost savings and enhanced efficiency of current linkage processes for cohort studies and follow-up for clinical trials. The FDA also would benefit from post-marketing surveillance, and cancer registries would be assisted with eliminating duplicate cases and accurately assessing multiple primary incidence.

Questions and Answers

Dr. Roach commented on the USPSTF's recommendations to not use prostate-specific antigens (PSAs) for prostate cancer screening even though evidence suggests its utility as a prognostic factor in treatment, and he expressed concern that PSA values from numerous trials are not included in SEER. Dr. Penberthy replied that a quality assurance study of SEER identified an error rate in PSA associated with an implied decimal point; 2012 data have been reviewed and corrected, and data back to 2004 will be re-entered with the assistance of natural language processing. She added that calculations to determine the impact of PSA on staging used the most recent staging system and found that only 1 to 3 percent of cases were affected.

Dr. Charles L. Sawyers, Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, Investigator, Howard Hughes Medical Institute, and Professor of Medicine, Weill Cornell Medical College, encouraged the NCI to leverage pharmacy relationships to use time-on-therapy as a proxy for time-to-progression, particularly for oral medications, and he asked about the ability to obtain these data while maintaining privacy rights. Dr. Penberthy clarified that cancer surveillance data are exempt from the privacy rules of the Health Insurance Portability and Accountability Act (HIPAA).

In response to a query by Dr. Joe Gray, Dr. Penberthy answered that the standards for acquisition and presentation of surveillance data have existed for many years, and SEER is in the process of evaluating guidelines and standards of care to identify those specific data elements (e.g., whole exome sequencing data) that are critical to collect. Dr. Gray encouraged obtaining consensus from the broader biomedical community regarding new standards.

Dr. Jonathan M. Samet, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine, and Director, Institute for Global Health, University of Southern California, encouraged the NCI to reflect on its underlying design for the proposed SEER concepts, which could be seen as involving a cohort study of millions of people at a time with 400,000 new entries into the cohort annually, and to consider nested sampling approaches to ensure quality data are obtained.

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Washington University School of Medicine, suggested that input from an IRB be obtained early in the development of the SEER concepts to ensure their feasibility for registries.

Dr. Basch commended SEER for its impact and linkages to biologic and genomic data and recommended that training be provided to build the next cadre of analysts and investigators who can conduct rigorous analyses as data become available. He asked how linkages may bypass the need to directly engage private payers to obtain data for those younger than age 65 and encouraged greater standardization of data collection by the states to support the concept of the mega-virtual repository.

Dr. Kenneth C. Anderson, Kraft Family Professor of Medicine, Harvard Medical School, and Director, Lebow Institute for Myeloma Therapeutics, Dana-Farber Cancer Institute, expressed concerns about the quality of the data available from EHRs and encouraged the NCI to consider a pilot project to estimate the cost of the outcomes shown in the registries. Dr. Penberthy noted that pharmacy transaction switchers retain data on transactions that have not been completed, providing an opportunity to consider cost barriers for some oral drugs. She also referred to an ongoing pilot study with linkages of secondary data specifically to assess financial toxicity and examine modeling predictors of financial toxicity in patients.

Dr. Cullen encouraged the NCI to take advantage of opportunities for cost savings through shared efficiencies with the National Cancer Data Base (NCDB), which is co-funded by the American College of Surgeons (ACOS) and the American Cancer Society (ACS), and other large registries.

VIII. A 1-DOSE/2-DOSE HPV VACCINE TRIAL—DR. AIMÉE KREIMER

Dr. Stephen Chanock, Director, Division of Cancer Epidemiology and Genetics (DCEG), introduced Dr. Aimée Kreimer, DCEG, who presented a randomized control trial (RCT) in Costa Rica to determine if a single dose of the prophylactic HPV vaccines would provide durable protection against cervical cancer. Dr. Kreimer stated that the global burden of cervical cancer is the greatest in developing countries and that current global vaccination patterns will yield only a marginal reduction on cervical cancer. Quadrivalent and nonavalent vaccines are licensed in the United States under a three-dose schedule for females and males ages 9–26, and a bivalent vaccine also is licensed for females. Members were told that HPV vaccination of naïve individuals results in nearly 100 percent protection against both incident HPV infections and cervical pre-cancer associated with vaccine-targeted HPV types. Dr. Kreimer noted that because HPV natural history follows a sexually transmitted disease pattern in which a steep increase in viral acquisition shortly follows sexual debut and diminishes as a woman ages, the goal of HPV vaccination is to eradicate the peak of HPV acquisition for one to two decades after sexual debut.

The NCI conducted an HPV vaccine trial in Costa Rica 10 years ago and enrolled 7,500 women, of whom 20 percent did not receive the full three-dose regimen. This allowed a post hoc analysis of the bivalent HPV vaccine stratified by the number of doses received, in which one and two doses showed vaccine efficacies that were comparable to three doses. Antibody data among these same women also support this finding and demonstrated stable antibody levels out to 4 years after vaccination for all dose groups. Dr. Kreimer described a trial in India intended to compare two- and three-dose efficacy, but which resulted in a one-dose arm because of political suspension; indications after 3 years are that a single dose may induce protection similar to that seen in Costa Rica. Preliminary findings in a 7-year follow-up in Costa Rica suggest that protection afforded by one dose results in continued efficacy against virologic infections and sustained antibody titers out to 7 years. Members were told that although there is no precedent for a single dose of a subunit protein-based vaccine to confer stable serum antibody levels or long-term protection, data continue to accumulate that suggest one dose might be sufficient.

Dr. Kreimer stated that the new study would involve a four-arm trial to evaluate one and two doses of the bivalent and nonavalent HPV vaccines; an epidemiologic HPV survey to document HPV infection among unvaccinated girls; and immunobridging to accelerate implementation in other populations or using other vaccine formulations. A secondary objective is to compare sustained immune titers via measurement of serum antibodies between girls who received one and two doses of the HPV vaccines. A total of 5,000 adolescent girls would be recruited in each of the four arms. The epidemiologic HPV survey would include three study visits over 1 year, collect the same samples as the RCT, and offer HPV vaccination.

Members were informed of additional immunologic studies to establish the lowest serum antibody level that confers strong protection with a single dose, translate immunobridging studies to other populations, and conduct subsequent trials of biosimilar VLP-based HPV vaccines to be immunobridging trials. The NCI is also considering a companion one-dose/two-dose immunogenicity trial in the United States.

Dr. Kreimer stated that 4 years of strong protection in the trial is intended to provide the level of evidence needed to change policy and take advantage of opportunities to evaluate other populations and vaccine formulations. In addition, if successful, VLP-based vaccines should be considered in future vaccine development to reduce doses needed for protection. Longer term follow-up of the proposed trial would be needed to provide confirmation of duration of protection out to 10 years. Dr. Kreimer noted that herd immunity would result if sustained vaccine uptake was present in a population.

Questions and Answers

Dr. Shannon asked whether a completed trial in India would have produced adequate evidence to change policy. Dr. Kreimer responded that discussions with regulators have stressed the need to obtain evidence from an RCT, and not post-hoc analyses, to influence policy.

Dr. Cullen wondered about the possibility of monitoring oropharyngeal infection in candidates. Dr. Gerson asked about translation of the results to boys. Dr. Kreimer said that oral HPV occurs primarily in males and prevalence increases with age, thus it would be underpowered for assessment in a study of adolescent girls. She added that an immunobridging study could be conducted on immune responses by gender.

Dr. Olopade encouraged the accumulation of evidence through collaborations with the GAVI Alliance and other organizations to develop a cohort of vaccinated girls who could be followed for several decades and provide data to inform policy. Dr. Kreimer agreed that evaluating the totality of the evidence is critical, but cautioned about the need to maintain the rigor with which the data is being brought to inform the topic appropriately.

Dr. Daniel C. DiMaio, Waldemar Von Zedtwitz Professor and Vice Chairman of Genetics, Department of Genetics, Professor of Therapeutic Radiology and Molecular Biophysics & Biochemistry, and Scientific Director, Yale Cancer Center, Yale University School of Medicine, asked about efforts to include African populations. Dr. Kreimer replied that collaborations funded by European organizations are supporting immunogenicity studies in Tanzania, with plans to bridge to the new Costa Rica Trial. Specifically, samples will be tested by the FNLCR's immunology laboratory. She added that centralized testing of samples from diverse global regions will allow for immunobridging of results back to NCI's study in Costa Rica.

IX. EPSTEIN-BARR VIRUS VACCINES—DR. JEFFREY I. COHEN

Dr. Jeffrey I. Cohen, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases (NIAID), NIH, described experimental efforts to develop a vaccine against the Epstein-Barr virus (EBV). EBV is ubiquitous, with 95 percent of adults infected. Most primary infections in childhood are asymptomatic, but 75 percent of college students with primary EBV infection will develop infectious mononucleosis, and EBV-positive infectious mononucleosis increases the risk for Hodgkin lymphoma. EBV-associated malignancies in non-immunocompromised persons include gastric cancers; nasopharyngeal carcinoma; Hodgkin lymphoma; Burkitt lymphoma, particularly in Africa; and other malignancies (e.g., T-cell lymphoma, diffuse large B-cell lymphoma [DLBCL] of the elderly, and extranodal NK/T-cell lymphoma). In immunocompromised persons, EBV-associated malignancies include post-transplant lymphoproliferative disease (PTLD) in solid-organ transplant recipients, as well as Hodgkin lymphoma, Burkitt lymphoma, DLBCL, and primary central nervous system lymphoma in patients with HIV.

Vaccine candidates include the viral envelope glycoproteins gp350, gB, gp42, gH/gL, and BMRF2. Most vaccines have focused on gp350. The first study to show that a gp350-based vaccine might be effective was in cotton-top tamarins, which were protected against virus-induced malignant lymphoma. A single Phase 2, randomized controlled trial of a gp350 vaccine in healthy young adults demonstrated that the vaccine reduced the rate of infectious mononucleosis but did not prevent EBV infection. In a Phase 1 trial, T-cell peptide epitope EBNA-3A showed some suggestion of protecting against infectious mononucleosis. The rhesus lymphocryptovirus (LCV) model was selected to compare EBV vaccines. The study compared the efficacy of vaccines containing soluble rhesus LCV gp350; attenuated Venezuelan equine encephalitis virus replicon particles (VEE VRP) expressing rhesus EBV gp350; and VEE VRP expressing rhesus LCV gp350, EBNA-3A, and EBNA-3B. Soluble rhesus LCV gp350 induced the highest antibody levels after vaccination. Only the combination of VRP-gp350, EBNA-3A, and EBNA-3B induced rhesus LCV-specific CD4 and CD8 T-cell responses. Soluble gp350 protected best against EBV challenge, reducing the EBV DNA viral load, and also performed best at reducing rhesus EBV DNA more than 1 year after challenge. A vaccine that reduces EBV DNA viral load, even without preventing infection, might reduce the risk of certain EBV lymphomas, based on evidence linking decreased viral load to decreased EBV PTLD risk in transplant recipients.

Self-assembling nanoparticle-based vaccines were tested to improve on results from soluble gp350. Nanoparticle-based vaccines result in a multivalent, symmetrical, repetitive array of antigen to improve immunogenicity. Nanoparticles bound to domains 1, 2, and 3 of gp350 (ferritin-gp350) consisted of spheres with multiple glycoproteins radiating from the surface and binding sites spaced at optimal distances for B-cell receptor binding. Ferritin-gp350 induced higher B-cell neutralizing titers and higher levels of antibody to the CR2 binding site than soluble gp350 in mice. Ferritin-gp350 neutralizing antibody persisted longer than soluble gp350. In a challenge study, ferritin-gp350 protected mice against vaccinia virus expressing gp350. Ferritin-gp350 induced 100-fold higher B-cell neutralizing titers in mice than titers in seropositive humans.

Other EBV proteins were tested to determine whether they should be part of an EBV vaccine. The predominant cells infected by EBV differ by disease and involve different proteins for cell entry (i.e., gp350, gp42, gH/gL, and gB for B-cell entry, and BMRF2, gH/gL, and gB for epithelial cell entry). The implications for an EBV vaccine are that a multivalent EBV vaccine, including gp350 and gH/gL with or without gp42, might be developed to induce antibodies to neutralize infection of both B and epithelial cells. Ferritin-gH/gL and ferritin-gH/gL/gp42 particles (ferritin-gH/gL±gp42) were synthesized. Ferritin-gH/gL±gp42 induced higher neutralizing titers in mice for B-cell and epithelial cells than soluble gH/gL±gp42. Ferritin-gp350 and ferritin-gH/gL±gp42 also induced higher B-cell and epithelial cell neutralizing antibodies in mice than serum from EBV-positive humans. Comparing neutralization titers

for nanoparticle versus soluble glycoprotein, ferritin-gp350 was 100-fold higher for B-cell neutralization, and ferritin-gH/gL±gp42 was 10- and 15-fold higher for B-cell and epithelial-cell neutralization, respectively.

Potential EBV vaccine trials include prevention of infectious mononucleosis, post-transplant lymphoma, disease in boys with X-linked lymphoproliferative disease, Burkitt lymphoma in Africa, Hodgkin lymphoma, nasopharyngeal carcinoma, and gastric carcinoma. The EBV gp350 subunit vaccine might not induce sterilizing immunity, but it may reduce symptoms of infectious mononucleosis and limit viral load set point after infection, reducing the likelihood of PTLD and rates of EBV-associated malignancies.

Questions and Answers

In response to a query by Dr. DiMaio, Dr. Cohen said that because gH/gL is highly conserved, multiple different strains are not expected for a vaccine.

Dr. Sawyers wondered whether ferritin functions as a vehicle to display antigen in a more efficient way or targets the antigen to different parts of the body to generate a response. Dr. Cohen indicated that researchers surmise that the display of the antigen has led to the focusing of the immune system on developing neutralizing antibodies, thus allowing a crosslink with B-cell receptors. Dr. Lowy pointed out that the vaccine developed by Dr. Cohen's laboratory is by far the most advanced candidate EBV vaccine that has been developed. The NCI laboratory, which is a Good Manufacturing Practice (GMP) facility, is in the process of making components for both of those vaccines for use in early-phase clinical trials.

Dr. Dang asked about the timelines for moving the vaccine into clinical trials. Dr. Cohen replied that the gp350 component is under development with a GMP-grade vaccine anticipated within a year, Phase I HSV vaccine studies should commence at the Clinical Center soon, and the Vaccine Research Center (VRC) is planning a clinical trial with the ferritin component with Influenza HA in 2016. Dr. Jacks added that Cancer Research UK announced a series of grant challenges that include the elimination of EBV-associated cancer by prophylactic vaccination or other means.

Dr. Yuan Chang, American Cancer Society Research Professor, Distinguished Professor of Pathology, UPCI Chair of Cancer Virology, University of Pittsburgh Cancer Center, asked whether results similar to the gp350 in relation to lymphocryptoviruses would be seen with the gamma herpes viruses. Dr. Cohen clarified that lymphocryptoviruses in different models have gp350s but differ in other areas, and he added that they can substitute for each other in some areas.

X. RFA/COOPERATIVE AGREEMENT CONCEPTS—NCI STAFF

Division of Cancer Biology and Division of Cancer Prevention

Barrett's Esophagus Translational Research Network— Dr. Rihab Yassin and Ms. Ellen Richmond

Dr. Rihab Yassin, Program Director, Cancer Cell Biology Branch, Division of Cancer Biology (DCB), and Ms. Ellen Richmond, Nurse Consultant and Program Director, Gastrointestinal and Other Cancer Research Group, Division of Cancer Prevention (DCP), presented the concept for a Request for Applications (RFA) reissuance to continue funding the Barrett's Esophagus Translational Research Network (BETRNet). BETRNet is a multidisciplinary transdivisional program that addresses esophageal adenocarcinoma, a rare cancer with a survival rate of less than 20 percent. Although Barrett's esophagus

is a precursor lesion that confers a risk of 11- to 30-fold greater than average, 80 to 90 percent of esophageal adenocarcinomas have no prior diagnosis of Barrett's and few Barrett's cases progress to esophageal adenocarcinoma. The Network's research activities to address this challenging paradigm have included: (1) the development of a transgenic mouse model, which suggested that etiology involved a stem progenitor cell in the gastric cardia rather than the esophagus; (2) accelerated validation of the mouse model through the consortium; (3) the discovery, made possible by combining rare esophageal cancer specimens from multiple BETRNet institutions, of a protective role of the GSTT2 gene in the African American esophagus; and (4) the development of an alternative model through genomic doubling. BETRNet also has provided a coordinated outreach to the larger community to exploit the emerging ideas and engage external investigators and has developed a Patient Registry-Virtual Repository (PR-VR) to track specimen availability across the Network, with 4,000 specimens available for collaborative research study. An evaluation of the program by a special committee found that the BETRNet RFA provided the necessary infrastructure to support collaborative research to synergize science and accelerate opportunities for translational studies, could serve as a model for other adenocarcinomas that have undefined or inaccessible precursor lesions, and noted significant accomplishments of the Network, such as the epidermal growth factor receptor (EGFR) probe for clinical utility, as well as the epigenetics and exome sequencing study.

The reissue concept would support four multi-institutional, transdisciplinary research centers (U54) to support the collaborative accrual of sufficient cohorts/specimens that could not be collected at a single institution, as well as a collaborative approach to new research directions and expertise sharing, and a Coordinating Center (U24). Research questions would encompass such topics as cell of origin, the genomics of esophageal adenocarcinoma, microbiota, and technologies and models. An FY 2014 portfolio analysis revealed that although the intramural and extramural research programs focused on this cancer included R01, U01, and P01 mechanisms, as well as BETRNet, none represent the type of infrastructure provided by BETRNet to tackle these research questions collaboratively. Dr. Yassin described program evaluation metrics that would cover scientific understanding of esophageal adenocarcinoma formation; improved PR-VR availability to the scientific community; new research tools and technologies for patient management; and model organisms, genome-wide association studies (GWAS), data, and resource sharing.

Subcommittee Review. Dr. Dafna Bar-Sagi, Vice Dean for Science, Senior Vice President, and Chief Scientific Officer, Professor, Department of Biochemistry and Molecular Pharmacology, NYU Langone Medical Center, New York University School of Medicine, expressed the Subcommittee's support for the concept reissue with the expansion to etiologies of esophageal adenocarcinoma beyond Barrett's. Dr. Bar-Sagi noted that program staff adequately responded to the Subcommittee's concerns about the achievability of the program's goals and intended impact as well as about sharing resources between the Centers and with the external community. The Subcommittee encouraged the Network to consider research on hormonal and abdominal obesity influences in esophageal adenocarcinoma, particularly as a risk factor for men. The Subcommittee had concerns about the cell study and evaluation report's comments on the Network's moderate productivity and encouraged the program to enhance its metrics to better track the promotion of specimen usage for a collaborative research study. Furthermore, BETRNet should fully connect with researchers in the field who are external to the Network, particularly regarding the PR-VR biobank.

The first year cost is estimated at \$5.5M for four U54 awards and one U24 award, with a total cost of \$27.6M for 5 years.

Question and Answer

Dr. Wicha commented on the value of the biobank and the ability to mimic changes *in vitro* and share live tissue across universities for the cell-of-origin activity. Dr. Yassin agreed and remarked that linking the *in vitro* changes to the repository could provide another tool for researchers.

Motion. A motion to concur on the Division of Cancer Biology (DCB) and Division of Cancer Prevention's (DCP) request for application (RFA) reissue entitled "Barrett's Esophagus Translational Research Network (BETRNet)" was approved with 21 ayes, 0 (zero) nays, and 2 abstentions.

XI. ONGOING AND NEW BUSINESS—DR. TYLER E. JACKS

NCAB *Ad Hoc* Global Health Subcommittee. Dr. Olopade provided a report of the 30 November 2015 meeting of the *Ad Hoc* Subcommittee on Global Cancer Research and noted worldwide emphasis on assisting countries to have strategies for cancer control following strong declarations in 2011 by the World Health Organization (WHO) and United Nations on noncommunicable diseases, including cancer. The Subcommittee heard about the Center for Global Health's (CGH) strategic activities to advance cancer control in various countries, including by convening funders to implement cancer control policies. In addition, the NCI has worked to bring the global community together to control cancers that have infectious disease etiology, including through vaccinations for HPV and EBV. Updates also were provided on the NCI's initiatives addressing global tobacco and ecological niche cancers, as well as several RFAs to add supplemental funding to NCI-designated Cancer Centers and to develop Regional Centers of Research Excellence. The Subcommittee appreciated both the establishment and ability of the CGH to help focus scientists on certain niche areas for research, build partnerships, and contribute to the efforts of the WHO and other international organizations.

Questions and Answers

Dr. Deborah Watkins Bruner, Robert W. Woodruff Chair of Nursing, Nell Hodgson Woodruff School of Nursing, Associate Director for Outcomes Research, Winship Cancer Institute, Emory University, requested clarification about the CGH's highest priorities and impact in terms of the NCI's investment. Dr. Jacks said that the CGH operates with a limited budget and marked the issue for further discussion at a future NCAB meeting.

Dr. Adamson commented on the swell of barriers to collaborating globally within the National Clinical Trial Network (NCTN) and encouraged the NCI to consider a holistic approach to foster collaboration for global cancer research.

Motion. A motion to accept the report of the 30 November 2015 NCAB *Ad Hoc* Global Health Subcommittee meeting was approved unanimously.

Motion. A motion to establish a Tobacco Control Working Group was approved unanimously.

XII. NCAB CLOSED SESSION—DR. TYLER E. JACKS

This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c) (6), Title 5 U.S. code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2)."

There was a review of intramural site visits and tenured appointments, committee discussions, and recommendations. There also was a discussion of personnel and proprietary issues. Members absented

themselves from the meeting during discussions for which there was potential conflict of interest, real or apparent.

XIII. ADJOURNMENT—DRS. TYLER E. JACKS AND CHI V. DANG

There being no further business, the 6th joint meeting of the BSA/NCAB was adjourned at 4:30 p.m. on Tuesday, 1 December 2015.

Date

Chi V. Dang, M.D., Chair, BSA

Date

Tyler E. Jacks, M.D., Chair, NCAB

Date

Paulette S. Gray, Ph.D., Executive Secretary