

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
5TH JOINT MEETING OF THE BOARD OF SCIENTIFIC ADVISORS
AND THE NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
June 24, 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
June 24, 2015**

The Board of Scientific Advisors (BSA) and the National Cancer Advisory Board (NCAB) convened for the 5th Joint Meeting on 24 June 2015, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Wednesday, 24 June 2015, from 8:30 a.m. to 4:25 p.m., and closed to the public from 4:30 p.m. to 5:30 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, presided during the open session. In the absence of Dr. Todd R. Golub, Chief Scientific Officer, The Broad Institute of Harvard University and Massachusetts Institute of Technology, Dr. Jacks served as the *pro tem* Chair of the BSA. Dr. Jacks presided during the closed session.

BSA Members

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

NCAB Members

Dr. Tyler E. Jacks (Chair)
Dr. Peter C. Adamson
Dr. Deborah Watkins Bruner
Dr. Yuan Chang (absent)
Dr. David C. Christiani
Dr. Marcia R. Cruz-Correa
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 (absent)
Dr. Charles L. Sawyers (absent)
Dr. William R. Sellers (absent)
Dr. Max S. Wicha

Alternate Ex Officio NCAB Members

Dr. Robert T. Anderson, DOE
Dr. Michael A. Babich, CPSC
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS
Dr. Richard Pazdur, FDA
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)
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, Acting Director for Clinical Research, Division of Cancer Treatment and Diagnosis
Dr. Lynn Austin, Executive Officer, Deputy Director for Management
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 Assistant for Science Planning
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. Glenn Merlino, Acting Scientific Director for Basic Research, Center for Cancer Research
Dr. Alan Rabson, Deputy Director, National Cancer Institute
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. Maureen Johnson, Executive Secretary, Office of the Director
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy

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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WEDNESDAY, JUNE 24, 2015

I. CALL TO ORDER AND OPENING REMARKS—DR. TYLER E. JACKS

Dr. Jacks called to order the 5th 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. Dr. Jacks reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the 11 March 2015 BSA meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. TYLER E. JACKS

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

Motion. A motion to confirm the future meeting dates for the BSA and NCAB for 2015 and 2016 was approved unanimously.

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

Dr. Douglas R. Lowy, Acting Director, welcomed and thanked members for attending despite the inclement weather across the United States. He provided an update on the status of NCI programs. Members were informed that the first recipients of the Outstanding Investigator Award (OIA) will be announced in the next few weeks. Dr. Lowy told members that the OIA provides long-term support to experienced investigators with outstanding records of cancer research productivity who propose to conduct exceptional research, and it allows them the opportunity to take greater risks, be more adventurous in their lines of inquiry, and take the time to develop new techniques.

Dr. Lowy reminded members that President Barack Obama has proposed \$70 million (M) in his fiscal year (FY) 2016 budget for the Precision Medicine Initiative in Oncology (PMI-Oncology). The NCI's approach to PMI-Oncology will be discussed later in the meeting, and a future workshop will explore the translational potential for the specific reactivation or replacement of tumor suppressor gene activities. PMI-Oncology concerns cancer screening and prevention, as well as treatment. Members were informed that the NCI is emphasizing screening based on application to molecular diagnostics, rather than pattern recognition. For example, in cervical cancer screening, cytologic or Pap smear screening is more sensitive for detecting squamous cell cancer precursors than for detecting adenocarcinoma precursors; a substantial decrease in squamous cell cancer incidence at the cervix has not been found in adenocarcinoma. A study published recently in *The Lancet*, which combined four randomized controlled trials conducted in Europe, found that human papillomavirus (HPV) testing can prevent more cervical cancers, especially adenocarcinomas, than cytology. Aspirin has shown similar results in reducing the risk of several cancers, particularly colorectal cancer. Molecular understanding can be used to risk-stratify those patients who will derive the greatest benefit from aspirin, thus increasing the benefit/harm ratio and addressing concerns about side effects of aspirin that have prevented its recommendation for reducing cancer risk. Members were reminded that the NCAB had previously heard data from Dr. Andrew Chan showing that high 15-hydroxyprostaglandin (15-HPGD) in the normal colon is associated with reduced risk of colorectal cancer in regular aspirin users.

Members were informed that another area of NCI interest is specific cancers with health disparities, as these represent high-risk populations. Dr. Lowy stated that the NCI will identify specific

cancers, such as colorectal, liver, breast, and prostate cancers; identify risk factors and their relative contribution to disparities, including biological and lifestyle factors, as well as health care access and utilization; and explore efforts to mitigate those risk factors. He referred to a study published in *Proceedings of the National Academy of Sciences (PNAS)* that found 15 novel recurrently mutated genes in colon cancer among African Americans, but not in Caucasians, suggesting an important difference in the mutational landscapes arising in various ethnic groups. Access to minority populations is important for such studies, and the NCI's efforts to include underrepresented minorities in the NCI Cooperative Group Clinical Trials during the past 5 years have resulted in approximately one in five patients being minority individuals.

Strong Support for Basic Research and the NCI Budget. Dr. Lowy emphasized the NCI's continued strong support for basic research that can elucidate important processes that lead to cancer. He described the declining purchasing power of the NCI budget, which had doubled between 1999 and 2004 and seen an appreciable increase in 2009–2010 because of the American Recovery and Reinvestment Act of 2009, which helped to support The Cancer Genome Atlas (TCGA) Project. In inflationary terms, however, the NCI's current purchasing power is similar to that of 1999. Dr. Lowy expressed cautious optimism about increases in appropriations for the NCI and NIH for FY 2016.

Members were told that 1,200 new competing research project grants were awarded in FY 2014, more than the 1,100 awards made in each FY 2012 and 2013, and that the NCI is committed to maintaining this number. Dr. Lowy noted that the appropriation to the NCI decreased 5 percent in FY 2013 because of sequestration. He described several financial and demographic changes instituted by the NCI, including a decrease in the automatic cuts to the modular R01 grants from 17 percent to 8.5 percent, and an increase in both the average size of the OIAs and their length, from 5 years to 7 years.

NCI-Designated Cancer Centers. Dr. Lowy remarked on the recommendations of the Cancer Centers Working Group and expressed the NCI's commitment to increase the total amount of the P30 core grants starting in FY 2016, with initial focus on the Centers with the lowest size grants and a long-term goal of increasing the funding pool from \$255 M to \$300 M.

RAS Project. Dr. Lowy informed members that the RAS Project, which is managed by the Frederick National Laboratory for Cancer Research (FLNCR), is producing validated gateway entry clones for 180 genes, or a total of 360 clones, of which 17 were not available commercially and 32 were not available without non-silent mutations. The clones will be made available to the community, and requests can be sent to Dr. Dom Esposito, FNLCR (espositod@mail.nih.gov).

FNLCR Recompetition. Dr. Lowy stated that the NCI has announced the recompetition for the Operations and Technical Support contract that runs the NCI Federally Funded Research Development Center known as the FNLCR. Leidos Biomedical Research currently administers the contract. Information concerning the competitive process will be announced on FedBizOpps and the FNLCR Acquisition Portal, with a pre-proposal conference scheduled for early October 2015. Members were told that the NCI will ensure a fair and open contract competition.

Personnel Changes. Members were informed of the retirements of Dr. Robert Wiltout, Director, Center for Cancer Research (CCR), in July; Dr. Joseph Tomaszewski, Co-Director, Division of Cancer Treatment and Diagnosis (DCTD), in May; and Ms. Susan Erickson, Office of Government and Congressional Relations (OGCR), in May. New appointments include Dr. Toby Hecht, Deputy Director, DCTD; Dr. Lee Helman, Acting Director, CCR; Dr. Glenn Merlino, Acting Scientific Director (Basic Section), CCR; Ms. M.K. Holohan, Acting Director, OGCR; and Mr. Peter Garrett, Director, Office of Communications and Public Liaison (OCPL).

Center for Global Health (CGH). Dr. Lowy introduced Dr. Marie Ricciardone, newly recruited to the CGH. Dr. Ricciardone is a molecular biologist who previously was a professor at Bilkent University in Ankara, Turkey, and whose husband served as the U.S. Ambassador to Turkey.

NCI Outreach. Members were referred to a new version of the NCI's website (www.cancer.gov), which is now compatible with smartphones, and were encouraged to review and share feedback on it. Dr. Lowy commended Dr. James H. Doroshow, Deputy Director, on the recent opening of the NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) Trial and the notable media interest in the project. He also expressed appreciation for members' input and reflected on the importance of the NCI's work to help patients live longer, healthier lives by decreasing the incidence of cancer and improving the outlook for patients who develop cancer.

Questions and Answers

Dr. Jacks requested further information about the recompetition of the FNLCR. Dr. Lowy said that the Frederick National Laboratory Advisory Committee (FNLAC) has provided guidance about the direction of the FNLCR, influenced by a visit to the U.S. Department of Energy's (DOE) Lawrence Berkeley National Laboratory, which operates as a partnership between corporate and academic entities. Enthusiasm continues for FNLCR programs, including the RAS Project and NCI Experimental Therapeutic (NExT) Program.

Dr. Elizabeth M. Jaffee, The Dana and Albert "Cubby" Broccoli Professor of Oncology, Co-Director of the Gastrointestinal Cancers Program, and Associate Director for Translational Research, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, asked about NCI's activities in cancer immunology and inflammation. Dr. Lowy recognized the importance of these areas for both the pathogenesis and treatment of cancer and expressed the NCI's aim to complement private-sector studies in these areas by elucidating immune and inflammatory mechanisms.

IV. PRESIDENT'S CANCER PANEL REPORT—DR. BARBARA K. RIMER

Dr. Barbara K. Rimer, Dean, Gillings School of Global Public Health and Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, provided a report on the recent activities of the President's Cancer Panel (PCP, the Panel). Dr. Rimer stated that the mission of the PCP is to identify barriers to progress of the National Cancer Program and communicate them to the President of the United States. In addition to Dr. Rimer, the Panel members include Dr. Owen N. Witte, University of California, Los Angeles, and actor Hill Harper. Dr. Rimer reported on outcomes stemming from the PCP's 2012–2013 Report to the President, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer," to which Drs. Lowy and Harold Varmus provided input, and the status of the current 2014–2015 workshop series, "Connected Health: Improving Patients' Engagement and Activation for Cancer-Related Health Outcomes."

By working closely with a number of key organizations, such as the Centers for Disease Control and Prevention, the American Cancer Society and the National Vaccine Advisory Committee (NVAC), the PCP was able to secure commitments to a number of their recommendations before the report was released. A broad coalition of public, private, and voluntary organizations is collaborating to increase HPV vaccination coverage and agreed at the first meeting of the National HPV Vaccination Roundtable in February 2015 that all pilot projects implemented by the Roundtable must be responsive to the PCP's HPV report recommendations. In June 2015, the National Vaccine Advisory Committee (NVAC) approved the five recommendations of the NVAC HPV Working Group, which included endorsing the Panel's HPV report and adopting its recommendations. In addition, the NVAC HPV Working Group endorsed monitoring the uptake and implementation of PCP recommendations, and urged that the

Assistant Secretary for Health develop relevant communications strategies to increase HPV vaccine uptake. Members were informed that the NCI is conducting intramural and extramural research on the HPV vaccine that is responsive to the Panel's recommendations. Dr. Lowy stated that another NVAC recommendation for a large-scale trial to evaluate two- and one-dose regimens of the two approved HPV vaccines would have benefits for costs, logistics, and uptake. Dr. Abby Sandler, NCI, will provide the keynote address on the PCP's HPV report at the November 2015 Cancer Prevention & Research Institute of Texas conference.

Members were informed that the PCP's 2014–2015 workshop series addresses the potential of connected health to improve cancer-related outcomes. Dr. Rimer explained that the workshop series included a planning meeting in June 2014, as well as workshops on engaging patients in Boston in December 2014 and on personal health data and cancer in San Francisco in March 2015. Participants at the workshops discussed opportunities provided by connected health to improve patient outcomes, the need for connected infrastructure to support team care and precision medicine, and the advantages of connected care in facilitating patient participation in clinical trials and diminishing disparities in care and health outcomes. A third workshop is planned for Chicago in July 2015 to identify recommendations to achieve a future state that would be beneficial to patients and the public by focusing on personal health information and data sharing, person- and family-centered care, optimal use of devices, and the National Health Information Infrastructure, including opportunities to use patient-reported outcomes (PROs) in a proactive way. Dr. Rimer was joined by Dr. Brad Hesse, Division of Cancer Control and Population Sciences (DCCPS), who described fractures in the foundations of cancer care that could be addressed by connected health, including: primary prevention (e.g., follow-up for smokers), secondary prevention (e.g., uptake of screening in the community health system), treatment adherence, and communication problems experienced by cancer survivors. Future stresses in oncology that may worsen these fractures include aging demographics, higher incidence rates, more complex oncology care, an increasing number of survivors, a shrinking workforce, and rising treatment costs. The health care communication revolution provides opportunities to bridge gaps by fixing patient handoffs, utilizing new communication technologies, smart scheduling, and secure messaging, and better leveraging eHealth to move care to patients. Members were told that following the 2014–2015 series of workshops, the PCP will review the input that it has received, conduct additional research as needed, and prepare a report to the President.

Questions and Answers

Ms. Mary L. Smith, Co-Founder, Research Advocacy Network, asked whether the ways in which behavioral change can be achieved had been discussed. Dr. Rimer confirmed that behavioral change had been part of the discussions.

Dr. Ethan M. Basch, Associate Professor of Medicine, Division of Hematology/Oncology, and Director, Cancer Outcomes Research Program, The University of North Carolina at Chapel Hill, observed that connected health offers opportunities to leverage tools developed from research, as well as to use tools from clinical practice in research, such as the NCI Patient-Reported Outcomes Measurement Information System (PROMIS). He also noted the need for quality metrics to assess engagement and connectivity of patients with providers and between the research and patient worlds. Dr. Rimer agreed and said that research tools, such as visualization, could be valuable for patients and their doctors to track progress; quality metrics also are needed, and the effects of social media should be studied. Dr. Hesse added that connected health provides opportunities to locate the breakdown points in patient care.

V. CENTER FOR CANCER RESEARCH AND FOOD AND DRUG ADMINISTRATION COLLABORATION—DR. RICHARD PAZDUR

Dr. Richard Pazdur, Director, Division of Hematology and Oncology Products, U.S. Food and Drug Administration (FDA), presented a joint FDA-NCI program to recruit clinical investigators who will perform clinical and regulatory duties for the two organizations. Dr. Pazdur was joined by fellow presenters, Drs. Sanjeeve Balasubramaniam, FDA; and Lee Helman, Scientific Director for Clinical Research, CCR. The program is to fill positions that will be joint appointments at the CCR and FDA's Center for Drug Evaluation and Research (CDER)/Office of Hematology and Oncology Products (OHOP). Members were informed that investigators will be FDA employees and will become expert in regulatory processes focusing on a specific disease type, from the Investigational New Drug (IND) application to the non-disclosure agreement (NDA) and post-marketing, and will develop a pivotal role in guiding industry and academia in their approach to drug development. At the NCI, the investigators will collaborate with existing clinical teams in the development and execution of clinical trials, the enrollment of patients, and the analysis and publication of data, as well as serve as a sounding board for clinical trial design. Mid-career clinical investigators with clinical trial experience are sought, particularly those with expertise in a particular disease area in hematology/oncology and interest in maintaining an active clinical research career while developing regulatory expertise in oncology. Dr. Balasubramaniam stated that in response to changes in the clinical regulatory pathway, which now include pharmacodynamics evaluation and biomarkers (Phase 0), safe dose (Phase 1a), dose expansion for specific populations (Phase 1b), and randomized accelerated approval (Phase 2), the OHOP reorganized in 2011 into disease-specific divisions to better support clinical trial design and facilitate a new drug development environment.

Members were told that the joint position will include titles from both organizations. An Associate Director at the OHOP receives regulatory training within the context of a multidisciplinary, disease-specific team; oversees a portfolio of drug and biologic products at all phases of development; leads meetings with industry and academic sponsors; represents the FDA to external stakeholders; and can conduct and publish regulatory science using the FDA's data and computing resources. Dr. Helman stated that a principal investigator (PI) at the CCR will collaborate within the Center; develop and submit clinical trials; conduct an estimated two to four actively accruing clinical trials; teach; and conduct investigator-initiated, industry, and cooperative group studies. Members were informed that the CCR includes 15 clinical oncology branches and provides substantial support throughout a protocol lifecycle, as well as support for technology transfer partnerships, research nursing, clinical care, core facilities, basic science, and data management.

Dr. Balasubramaniam stated that FDA/CCR clinical investigators would serve as leaders in the academic community, bringing disease-specific expertise, fulfilling unmet clinical needs at the FDA, and advancing efforts to modernize clinical trial design to align with the clinical community. Investigators would help the NCI design trials that establish and use new regulatory endpoints, such as alternatives to current surrogates or dose-finding schema, as well as expand inclusion criteria and highlight regulatory considerations in individual trials. Members were told that the FDA will serve as the chair of the search committee, and the CCR will participate in the search and selection of investigators.

Questions and Answers

Dr. Peter C. Adamson, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia, wondered about the challenges in recruitment and retention of investigators at the mid-career level. Dr. Pazdur said that the ideal candidate would be an established investigator with a presence in a specific field. He added that the clinical work in the joint position ensures that it is remarkably different from other career positions at the FDA.

Dr. Max S. Wicha, Deputy Director, Taubman Institute, Distinguished Professor of Oncology, and Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan, encouraged the FDA and NCI leadership to consider the program as having a dual mission of training investigators who remain in the Federal Government for their career and those who leave for careers in the extramural community. 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, University of Chicago Pritzker School of Medicine, said that the efficacy of the training could be expanded by engaging extramural training programs.

Dr. Wicha suggested that recruiting experts in Phase 1 development would leverage the increased focus on immune therapies and pathways in drug development. Dr. Pazdur responded that recruitment is focused on finding the right candidate and not targeted to a specific cancer.

Dr. 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, Siedman Cancer Center, University Hospitals Case Medical Center, encouraged the FDA and NCI leadership to stress that this program will help develop a leading edge competency in technologies and approaches that could not be achieved otherwise.

VI. RECOGNITION OF RETIRING BSA MEMBERS—DR. DOUGLAS R. LOWY

On behalf of the NCI, Dr. Lowy recognized the contributions made by members of the BSA whose terms of office have expired. He expressed appreciation for their service and dedication over the course of their terms. Retiring BSA members are: Drs. Curt I. Civin, Director, Center for Stem Cell Biology & Regenerative Medicine, Professor of Pediatrics & Physiology, and Associate Dean for Research, University of Maryland School of Medicine; Betty Ferrell, Professor, Nursing Research and Education, Full Member, Cancer Control and Population Sciences Program, Comprehensive Cancer Center, City of Hope National Medical Center; Todd Golub, Chief Scientific Officer, The Broad Institute of Harvard University and Massachusetts Institute of Technology; Bruce W. Stillman, President and Chief Executive Officer, Cold Spring Harbor Laboratory; and Irving L. Weissman, Director, Institute of Stem Cell Biology and Regenerative Medicine, Stanford University.

VII. NCAB PHASE II CANCER CENTERS BUDGET WORKING GROUP REPORT—DR. STANTON L. GERSON

Dr. Gerson presented the findings in the NCAB Cancer Centers Working Group Report, Phase II: Streamlining the Cancer Center Support Grant (CCSG) Application and Evaluation Process. In its report, the Working Group—composed of nine Center Directors, four Associate Directors, and three NCI staff—aimed to improve and enhance the CCSG application and review process, amplify referees' ability to understand the importance and innovation of the Centers, remove and reduce the administrative burden, and streamline the process of application review. The Working Group began preparations in April and May 2014; divided into four working groups, conducted team teleconferences, and engaged in email dialogue from June through August 2014; assembled the final report in September and October of 2014; discussed the report at the Subcommittee A "Parent Committee" meeting in December 2014; and presented the report at the Cancer Centers Director's meeting in February 2015.

Members were informed that the Working Group unanimously approved the final report, which developed recommendations in four major areas. (1) Regarding the value and efficiency of the site visit, the report observed that other mechanisms do not have site visits, eliminating site visits would represent a significant time and cost savings for Centers and the NCI, and the scoring impact may balance out the results of the site visit. The report recommended eliminating site visit tours and poster presentations for

Shared Resources and replacing them with a question-and-answer session for Shared Resources. The Parent Committee reiterated the team-building value of the site visit for Centers and the opportunity provided by the site visit to answer questions better than written documentation. (2) Regarding clarity of the requirements and review criteria, the report recommended eliminating redundancy in the requirements for submission and review, restoring individual review of Shared Resources, and better defining eligibility requirements for the “comprehensive” designation to increase understanding by the Centers and reviewers. The Parent Committee commented that redundancy has some value for reviewers, individual review of Shared Resources is preferred, and added specificity may constrain Centers and reviewers. (3) The report recommended streamlining data collection by making greater use of direct data acquisition methods, progress on which is already occurring through the use of existing systems, such as the Clinical Trials Reporting Program (CTRP) and Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER); and using electronically available resources for biosketches. (4) To streamline annual CCSG progress reports, the report recommended simplifying the process by reducing their length and providing annually updated Data Tables to track progress. Dr. Gerson indicated that next steps include implementing changes to elements not defined in the CCSG funding opportunity announcement (FOA) and addressing other issues at the CCSG FOA reissue in September 2016.

Questions and Answers

Drs. Chi V. Dang, Professor of Medicine, Division of Hematology-Oncology, Department of Medicine, Director, Abramson Cancer Center, and Director, Abramson Cancer Research Institute, Perelman School of Medicine, University of Pennsylvania, and Kevin Shannon, Roma and Marvin Auerback Distinguished Professor in Molecular Oncology, American Cancer Society Research Professor, Department of Pediatrics, University of California, San Francisco, encouraged the NCI to provide guidance regarding the type of data or other content that would be most valuable to include in the Cancer Centers’ progress reports to better support the NCI’s mission.

Members expressed support for the inclusion of the site visit in the evaluation process as a means to galvanize the Cancer Centers. Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenbaum Cancer Center, Professor of Medicine, University of Maryland, observed that the site visit provides an impetus to focus investigators and program members within a Center on the broader landscape and positively affects the science that the Center produces. Dr. Cheryl L. Walker, Professor and Director, Institute of Biosciences and Technology, Center for Translational Cancer Research, and Welch Chair in Chemistry, Texas A&M Health Science Center, stressed the importance of onsite team interactions, as virtual reviews become more prominent.

Dr. Wicha asked why the site visit was made optional in the review process. Dr. Gray explained that several Cancer Centers previously had felt that they could go through the peer review process without the site visit; these Centers have since indicated that they would prefer having the site visits. Dr. Lowy stated that the NCI would be willing to implement changes provided that the review process remained rigorous and fair.

Dr. Adamson queried about refinements to the goal of the site visit, and Drs. Jacks and Gray responded that the site visit could be perceived as a part of the evaluation of the application. Dr. Gerson added that while site visits can help to improve applications, they should not be used to correct deficiencies. Dr. Dang confirmed that the Cancer Centers Working Group discussed whether the score before a site visit and after a site visit may have a substantive change or not.

Dr. Jaffee asked about ways to enhance the value of the site visit. Dr. Gerson responded that the Working Group had requested that the NCI help it to understand the value of the site visits and which parts are of most value.

Motion. A motion to express support that site visits be a mandatory part of the evaluation of NCI-designated Cancer Centers was approved with 30 ayes, 1 nay, and 1 abstention.

Motion. A motion to accept the report of the NCAB Phase II Cancer Centers Working Group Report was unanimous.

VIII. PRECISION MEDICINE INITIATIVE—DRS. JAMES H. DOROSHOW, LOUIS M. STAUDT, AND WARREN KIBBE

Dr. Doroshow provided an overview of the PMI-Oncology activity announced in President Obama's 2015 State of the Union Address. The President's Budget for FY 2016 allocates to the NCI a \$70 M net increase for its PMI activities, which focus on using genomics to identify and target molecular vulnerabilities of individual cancers. The PMI has four major goals: (1) expand genomics-based clinical and preclinical studies; (2) overcome, at the molecular level, resistance to targeted drugs and gain a mechanistic understanding of immunotherapy; (3) develop a large-scale, patient-derived, clinically annotated repository for evaluating targeted therapeutics; and (4) establish a national cancer database to integrate genomic information with clinical response and outcome. Dr. Doroshow informed members that a series of precision oncology trials were initiated in 2014: Molecular Profiling-Based Assessment of Cancer Therapy (NCI-MPACT); Lung Cancer Master Protocol (LungMAP); Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST); and Exceptional Responders. NCI-MATCH, a foundational trial that attempts to discover whether cancer treatment can be assigned based on molecular abnormality, launched in 2015 and will be available at 2,400 sites across the United States and also will serve as a regulatory umbrella. The NCI-MATCH trial is available for solid tumor patients and patients with non-Hodgkin's lymphoma; other immunologic malignancies will be added if resources become available. Future goals include establishing NCI-Pediatric MATCH and broadening the NCI-MATCH umbrella.

Dr. Louis M. Staudt, Director, Center for Cancer Genomics (CCG), elaborated on the need for precision medicine in oncology, noting that the current repertoire of cell lines is insufficient. Needed are patient-derived cancer models that recapitulate genotypes and phenotypes of human cancer cells to develop single and multidrug combinations that are specific to the characteristics of the tumors and to perform high-throughput small-molecule drug screening to identify new targets. Dr. Staudt expressed excitement about the accelerated pace of technological development for the study of functional dependencies. He noted that two new advancements—organoids and conditionally reprogrammed cells—hold promise for precision medicine. Dr. Staudt explained that the pilot phase of a human cancer model initiative would capture clinical data and produce, characterize, and make widely available new models. A 2-year contract is in place to create 1,000 new human cancer cell lines. The pilot has scientific, methodological, ethical, regulatory, and procedural considerations yet to be resolved, but a meeting to discuss operational details is planned for July 2015 at the NCI.

Dr. Warren Kibbe, Director, Center for Biomedical Informatics and Information Technology (CBIIT), described the Genomic Data Commons (GDC) and the NCI Cancer Genomics Cloud Pilots. The GDC is a single repository for all NCI cancer genomics data that will serve as a single platform for reharmonizing the data. Data will be freely available for download, subject to data access requirements. The NCI Cancer Genomics Cloud Pilots will explore approaches for meeting the research community's need to analyze large-scale cancer genomic and clinical data. The Cloud Pilots offer an opportunity to establish sustainable infrastructure, provide a data integration platform, and support clinical research focused on precision medicine. The NCI plans to expand and scale the GDC with community engagement and additional funding.

Questions and Answers

Dr. Marcia R. Cruz-Correa, Associate Professor of Medicine and Biochemistry, University of Puerto Rico, and Basic and Translational Science Director, University of Puerto Rico Comprehensive Cancer Center, asked about the potential for matching mechanistic information with chemoprevention studies and whether minority groups will be targeted within the 1,000-case goal. Dr. Doroshov replied that successful functioning of the national network infrastructure first needs to be ensured and that case accrual from minority-based NCI Community Oncology Research Program (NCORP) sites is expected to be robust.

Dr. Kenneth C. Anderson, Kraft Family Professor of Medicine, Harvard Medical School, and Director, Lebow Institute for Myeloma Therapeutics, Dana-Farber Cancer Institute, inquired about the path forward for inclusion of hematologic malignancies. Dr. Doroshov responded that multiple myeloma foundations and others have expressed interest, but resources are needed.

Dr. Dang requested identification of the deliverables in the pipeline. Dr. Staudt explained that the GDC will be available for use in May 2016 and that 1,000 cell lines should exist within a 2-year period (100–200 cell lines currently are available).

Dr. Shannon asked about extending the use of organoids to robust *in vivo* models of more common cancers. He also recommended using FNLCR resources for banking and characterization needs, as well as for resource dissemination to the community. Dr. Staudt acknowledged the loss of some subclonal heterogeneity in organoids but added that aspects of tumor microenvironment can be addressed.

Dr. Basch inquired about the collection of data on PROs. Dr. Jeff Abrams, Acting Director, DCTD, replied that PROs add complexity to trials with small numbers of patients, but that follow-on trials would integrate PROs. Dr. Deborah Watkins Bruner, Robert W. Woodruff Chair of Nursing, Nell Hodgson Woodruff School of Nursing, and Associate Director for Outcomes Research, Winship Cancer Institute, Emory University, encouraged the NCI to incorporate common patient experiences, adherence, and cognitive function performance status into the data collection.

Dr. Walker asked about the use of a centralized model versus a distributed model. Dr. Staudt explained that initially a concerted effort is needed to develop expertise, but researchers who have developed cell lines already have inquired about opportunities to share them.

Dr. Lincoln D. Stein, Director, Informatics and BioComputing Platform, Ontario Institute for Cancer Research, asked whether NCI-MATCH will be quantifying targeted mutations and developing germline material. Dr. Doroshov responded that exome sequencing and RNA sequencing will be performed on all patients; germline studies will not be pursued initially, but appropriate material will be collected.

Ms. Smith commented on the need to effectively communicate with investigators about patient enrollment. Dr. Doroshov responded that patient enrollment has and will vary in each of the phases.

Dr. Eileen P. White, Distinguished Professor, Department of Molecular Biology and Biochemistry, and Associate Director for Basic Science, Rutgers Cancer Institute of New Jersey, commented on the immune system's role in cancer and asked about the potential for reconstituting mice with both the tumor and immune system, suggesting the use of genetically engineered mouse models. Dr. Staudt stated that some approaches are working, for example, a humanized mouse that has many of the cytokines that support hematopoiesis. Dr. Jacks added that the PMI initiatives being discussed do not describe all of the NCI's interests; other programs address other important models.

Dr. Olopade suggested ensuring that the 1,000 planned cell lines are representative of the diverse domestic and global populations. Dr. Staudt agreed, noting that accepting samples from community-based programs is dependent on the feasibility of shipping samples overnight.

Dr. Sangeeta N. Bhatia, John J. and Dorothy Wilson Professor, Division of Health Sciences and Technology and Electrical Engineering and Computer Science, Institute for Medical Engineering and Science, Koch Institute for Integrative Cancer Research, Broad Institute, Brigham and Women's Hospital, Massachusetts Institute of Technology, pointed out the need for combination toxicity testing for target engagement in normal tissues and shared with members that the Tissue Chip for Drug Screening Program, supported by the National Center for Advancing Translational Sciences (NCATS), is seeking drug recommendations. Dr. Staudt stated that one goal is to make available normal organoids that can be used in parallel to address toxicities.

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Washington University School of Medicine, commented that large-scale patient databases could raise concerns about privacy. Dr. Kibbe acknowledged that some data cannot be made freely available and indicated that discussions about the topic continue.

IX. RFA/COOPERATIVE AGREEMENT CONCEPTS—NCI STAFF

Office of the Director

Non-Communicable Disease Regional Infrastructure Core Planning Grants (RFA)— Dr. Ted Trimble

Dr. Ted Trimble, Director, CGH, presented a concept to support activities for the planning and design of sustainable, regional research infrastructure cores (RICs) to address non-communicable diseases (NCDs) in low- and middle-income countries (LMICs) or regions. Dr. Trimble stated that LMICs are challenged in addressing NCDs, which share common risk factors—such as tobacco use, physical inactivity, unhealthy diet, harmful use of alcohol, and environmental factors—because of limited in-country support for research and training, inadequate research infrastructure, poor health care delivery services, lack of surveillance regard NCD management, and lack of coordination across relevant NCD activities. Members were told that many international studies conducted by organizations in the United States and the United Kingdom, including universities and Cancer Centers, operate in isolation. One notable exception is the Academic Model Providing Access to Healthcare (AMPATH), which provides a model partnership between Indiana University and Moi University in Kenya and a consortium of U.S. medical schools and other partners, including five NCI-designated Cancer Centers. The concept aims to establish partnerships similar to AMPATH, strengthen LMICs' commitment to public health research and implementation science, build an evidence base for NCD prevention and control, help build a global health career track for investigators focused on NCDs, and strengthen multidisciplinary research across NCDs.

Dr. Trimble said that this concept is for a planning phase that will be followed by two implementation phases. Activities of the planning grants include an assessment of NCD research needs and opportunities; encourage development of a consortium; development of a plan to coordinate research projects, infrastructure core development, and research training; and development of a strong application for core funding. An NCD RIC will include a partnership between a consortium of U.S. institutions and multiple LMIC institutions, the development of research core facilities, training and career development, and a focus on translating research into policy. Potential NIH partners include Fogarty International Center and other ICs to co-sponsor or make additional awards. Potential research areas span the cancer spectrum with a strong emphasis on implementation science and health disparities; core resources would

encompass effective grants and contracts management, research ethics oversight, bioinformatics and data management, health communications, and health economics and comparative effectiveness research. Evaluation criteria include the quality of the needs assessment, caliber of the research plan, a training plan, plans for the appropriate infrastructure cores, in-depth metrics, community engagement to identify the local research needs, strengthened administrative capacity of the LMIC institutions, and a credible plan for building a competitive research program. A network of NCD consortia is envisioned, as well as central NIH coordination led by the NCI.

Subcommittee Review. Dr. Basch expressed the Subcommittee’s strong enthusiasm for the concept, which was seen as a reasonable initial step toward establishing a network, provided that the two follow-on phases are adequately resourced. The Subcommittee appreciated that global oncology is a rapidly evolving field, NCDs are recognized as essential to address in developing nations, and many existing relationships between U.S. Cancer Centers and other organizations can be leveraged. Concerns were expressed about the level of funding for this stage of the program, coordination with other Institutes to ensure that the NCI investment remains relevant to oncology, and incentives to sites that have until now been autonomous to coordinate their efforts. The Subcommittee emphasized the importance of developing a collaborative infrastructure early to ensure productive activities and also encouraged a 3-year funding cycle to allow time to overcome challenges from geographic and daily processes.

The first year cost is estimated at \$2 M for six P20 awards, with a total cost of \$4 M for 2 years.

Questions and Answers

Dr. Adamson suggested that operations be included as a core resource and wondered about the level of global coverage possible with six planning grants. Dr. Trimble clarified that applications can focus on any region in the world, and the consortia likely would address a limited number of countries where a U.S. commitment already exists. He confirmed that the consortia can extend between countries.

Dr. Adamson asked whether consortia will need to include NCDs beyond cancer to be competitive, since cancer specific consortia already exist. Dr. Trimble explained that the concept is focused on NCD research, and added that the NCI is working on separate efforts to strengthen cancer-specific research networks, such as a Burkitt’s lymphoma network and a pediatric cancer network.

Motion. A motion to concur on the Center for Global Health’s request for application (RFA) entitled “Non-Communicable Disease Regional Infrastructure Core Planning Grants” was approved unanimously.

Clinical Proteomic Tumor Analysis Consortium (CPTAC) (Reissue RFA/Coop. Agr.)— Dr. Henry Rodriguez

Subcommittee Review. Dr. Bhatia expressed the Subcommittee’s support for the concept reissuance. Internal and external evaluations were favorable for reissuance, and the Subcommittee felt that the Program was productive in prior phases. The Subcommittee noted the Program’s three major contributions: development and sharing of techniques, tools, and standardization for rigorous proteomics; proteomic analysis of several key tumor types; and establishment of a framework to integrate proteomic and genomic data. Future efforts will include analysis of additional tumor types, as well as application of the tools to explore clinically relevant phenomena (e.g., drug sensitivity and resistance), which the Subcommittee considered to be an important and timely direction. The Subcommittee recommended heightened awareness of the Program to maximize its impact.

NCI’s Overview of Concept. Dr. Henry Rodriguez, Director, Center for Strategic Scientific Initiatives (CSSI), Office of Cancer Clinical Proteomics Research, informed members that CPTAC was

established to elucidate additional biology from deep proteomic analysis on genomically characterized tumors. A consortium of Proteome Characterization Centers (PCCs) coordinates standardized research activities and harmonizes analytical work flows and informatics to ensure high-quality data production and reproducibility. Through the U24 award, the PCCs provide data, assays, and reagents to the community. Members were informed that retrospectively collected biospecimens posed a major challenge in Year 1, because the effect of preanalytical variables, such as cold ischemia on protein measurement was unknown, and subsequently caused proteomic analysis to be postponed until the second year. Overall, CPTAC's investigations of colorectal, ovarian, and breast cancers have been successful and ongoing. The External Scientific Committee observed that the CPTAC structure has been successful and innovative at addressing proteomics cancer research and that CPTAC has accelerated the adoption of standardized proteomic approaches by the research community. It cautioned that innovative data analysis varied among PCCs and recommended avoiding retrospective samples, if possible.

Dr. Rodriguez explained to members that the reissuance concept has the following goals: (1) improve understanding of the proteogenomic complexity of tumors, with CPTAC's approach extending to five or six additional cancer types; and (2) apply CPTAC's analytically validated methodologies to clinical trials to address clinical and biological questions of drug response, toxicity prediction, and resistance. In addition to continuation of the PCCs for data generation, Proteogenomic Translational Research Centers (PTRCs) will conduct proteogenomic translation research on cancer models and clinical trial samples and Proteogenomic Data Analysis Centers (PGDACs) will develop innovative tools for data analysis across the entire proteome. It also will continue to provide resources to the community to accelerate proteomics science. He stated that the NCI has an opportunity to leverage its investments in cancer genomics by building on current achievements in cancer proteomics.

The first year cost is estimated at \$4 M for three U24 PCC awards, \$4.5 M for three U01 PTRC awards, and \$4.5M for four U01 PGDAC awards, with a total cost of \$20 M for PCCs, \$22.5 M for PTRCs, and \$22.5 M for PGDACs for 5 years.

Questions and Answers

Dr. Wicha suggested concentrating on single-cell analysis of individual tumors because a major barrier to treatment is tumor heterogeneity. Dr. Rodriguez responded that CPTAC has analyzed small sections of tumors using laser capture microdissection. Dr. Shannon suggested integrating diagnosis relapse tumor samples as well as diagnosis response tumor samples into the initiative.

Dr. Anderson asked about the potential for exploiting clinical annotation technology by collaborating with ongoing trials regarding precision medicine. Dr. Doroshow replied that relevant assays to ongoing NCI trials regarding precision medicine will be explored by CPTAC investigators.

Motion. A motion to concur on the Office of Cancer Clinical Proteomics Research's re-issuance request of RFA entitled "Clinical Proteomic Tumor Analysis Consortium (CPTAC)" was approved unanimously.

Genome Data Analysis Network (GDAN) (Reissue RFA/Coop. Agr.)—Dr. Louis M. Staudt

Subcommittee Review. Dr. Stein expressed the Subcommittee's support for the concept reissuance. He informed members that the GDAN is an extension of TCGA's Genome Data Analysis Centers (GDACs), which provided much of the computational backbone for TCGA. Collectively, GDACs have resulted in a large number of high-impact publications that encompass fundamental biological discoveries in the genomics of cancer, as well as a new generation of widely used algorithms. The Subcommittee felt that the RFA would benefit from enhanced discussion of (1) clinical correlation, (2) the integration of GDAN with precision medicine initiative and other large-scale genome-scale NCI

programs, and (3) community engagement in benchmarking and the selection of best current analysis tools.

NCI's Response to Subcommittee. (1) Dr. Staudt stated that integrating GDAN with clinical trials is critical to ensuring that new clinical correlations are found and validated in a statistically sound way. He agreed that clinical correlation should be highlighted as a core expertise. (2) Dr. Staudt stated that the GDAN will be involved in precision medicine as well as other CCG initiatives. A platform has been developed to process samples through the Biospecimen Core Repository, and a genome characterization contract is in place to generate primary data. Dr. Staudt lauded the TCGA as exemplary of team science and envisioned the GDAN as the core of the TCGA Analysis Working Groups that will be part of every project. (3) Dr. Staudt emphasized that community input is welcomed. The NCI Genomic Data Commons (GDC) will be the core database and knowledge base for all of GDAN's studies and will include both the raw data and the first level of analysis. An external advisory group and the Global Alliance for Genomics and Health (GA4GH) Data Working Group are engaged to help with choosing technologies, standards, and methods.

The first year cost is estimated at \$8.5 M for 14 U24 awards, with a total cost of \$45.5 M for 5 years.

Questions and Answers

Dr. Kevin P. White, James and Karen Frank Family Professor, Department of Human Genetics, Professor, Department of Ecology and Evolution, Director, Institute for Genomics and Systems Biology, Knapp Center for Biomedical Discovery, The University of Chicago, asked about a potential mechanism to ensure that specialized GDACs include community engagement. Dr. Staudt responded that bi-yearly TCGA meetings have included individuals from the GDC and plan to include representation from GDAN, individuals working in computational genomics, and others interested in genomics to help determine an agenda that would favor interaction between groups.

Motion. A motion to concur on the Office of the Director's (OD) re-issuance request of the RFA/Cooperative Agreement entitled "Genome Data Analysis Network (GDAN)" was approved unanimously.

X. U.S. NCI-CHINA RESEARCH COLLABORATIONS—DRS. TED TRIMBLE, LEE HELMAN, XIN WANG, ROBERT CROYLE, BRITT REID, STEPHEN J. CHANOCK, CHRISTIAN ABNET, BARRY KRAMER, YOU-LIN QIAO, AND YU WANG

Introduction. Dr. Trimble introduced a presentation on the U.S.-China partnership in cancer research, including the role of the CGH. The door between the United States and China was opened in 1971 with the meeting between Chairman Mao Zedong and President Richard Nixon. In 1979, Chairman Deng Xiaoping and President Jimmy Carter signed the U.S.-China Agreement on Cooperation in Science and Technology. The NCI Office of China Cancer Programs, dedicated to strengthening NCI's collaborations with China, was formed in 2008. China has much higher mortality rates from lung, stomach, liver, and esophageal cancer than the United States. Notably, Chinese women have remarkably high mortality from lung cancer, despite having low smoking rates. The NIH has jointly funded partnerships with the National Science Foundation of China (NSFC)—including projects with the National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), and National Institute of Neurological Disorders and Stroke (NINDS). The NIH also is collaborating with the Chinese Ministry of Science and Technology to explore opportunities for research, as well as to strengthen governance and peer review activities. With regard to training and capacity building, many Chinese postdoctoral fellows and researchers have visited and trained at the NCI, NCI-designated Cancer Centers, and universities.

Dr. Trimble introduced the presenters: Drs. Lee Helman, Scientific Director for Clinical Research, CCR, NCI; Xin Wei Wang, Deputy Chief, Laboratory of Human Carcinogenesis and Head, Liver Carcinogenesis Section, CCR; Robert Croyle, Director, DCCPS; Britt Reid, Deputy Associate Director, Epidemiology and Genomics Research Program, DCCPS, NCI; Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics (DCEG); Christian Abnet, Acting Chief, Nutritional Epidemiology Branch, DCEG, NCI; Barry Kramer, Director, Division of Cancer Prevention (DCP); You-Lin Qiao, Professor and Director, Department of Cancer Epidemiology, National Cancer Institute, Chinese Academy of Medical Sciences; and Yu Wang, Director-General, Chinese Center for Disease Control and Prevention.

Center for Cancer Research. Dr. Helman described connections with China at the CCR. Ten percent of CCR PIs are of Chinese descent. More than 150 recent alumni over the past 5 years are now working in China, primarily in academia (82%), but also in industry (11%). In 2014, 18 different PIs had active collaborations with 33 Chinese investigators at 28 different institutions, studying liver cancer, bladder cancer, neuroblastoma, and other cancers. The CCR has participated in and organized symposia in China, and the CCR is very involved with the U.S.-China Program for Biomedical Research Cooperation.

Dr. X. Wang stated that liver cancer is the second leading cause of cancer-related deaths worldwide, with the majority of new cases occurring in China, and has a very high mortality rate. Liver cancer is heterogeneous in its clinical presentation, demographics, environmental risk factors (e.g., HBV, HCV, chemical carcinogens), and lifestyle risk factors, which leads to highly heterogeneous tumor biology, both in genomics and the microenvironment. Collaborative studies of liver cancer between the NCI and Fudan University began in 1999. Pilot studies with Drs. Zhao-You Tang and Dr. Lun-Xiu Qin led to joint papers and the planning of larger studies, including a genome-wide association study (GWAS). A systems biology strategy to improve outcomes for liver cancer patients will involve developing a biobank and creating an information commons with omics-based classifications, leading to biomarker-guided interventions. Major accomplishments in research on liver cancer include proof-of-concept that the ability to metastasize may be an inherent quality of the primary tumor, which led to the development of the HeproDX test; a study showing the contribution of the tumor stroma to progression; the discovery of a gender-related biomarker, miR-26, which predicts response to interferon therapy; and the use of molecular and bioinformatics strategies to define liver cancer subtypes and drivers, which are potential targets. Collaborative studies between the NCI and Fudan University have been very productive, leading to more than 20 peer-reviewed publications, seven patents or patent applications, and multiple grants and awards. Challenges that remain include better defining tumor molecular subtypes; translating research findings to the clinic; evaluating less-studied risk factors (e.g., diet, lifestyle, liver fluke); addressing health disparities and global health; fostering bench/clinical/multi-institutional collaborations, such as the NCI-sponsored liver consortium; and addressing the limited funding and resources that are available for research and biobanks for a disease that is becoming more important in the United States.

Division of Cancer Control and Population Sciences. Dr. Croyle commented that the scientific opportunity represented by collaboration with China can be summed up as a greater range of exposure. DCCPS has four main research programs: epidemiology and genomics, surveillance, behavioral science, and health care delivery research, with epidemiology being the largest area of collaboration with China and an area in which increasing numbers of staff are working on issues of global health. Behavioral research and epidemiology and genomic research comprise the majority of the DCCPS grant portfolio, but health care delivery research is a growing funding area.

Dr. Reid reviewed some of the infrastructure and consortia collaborations between DCCPS and China. Mutual scientific interests include environmental exposures in cancer risk, genetic variance in

cancer risk, and tobacco control. DCCPS has a large and active portfolio of grants and cooperative agreements among Chinese populations with a variety of outcomes, including incidence of breast, colon, prostate, and other cancers. Critical cohorts include the Shanghai Women's Health Study (SWHS), Shanghai Men's Health Study, and Shanghai/Singapore Cohort. The SWHS was established in 1996 and has 75,000 participants with 5,000 incident cases; it has supported many junior investigators, it has resulted in more than 200 published manuscripts, and its resources have been used in more than 20 GWAS. SWHS investigators identified a new locus for breast cancer with relatively high frequency and a large effect size, and they established the Asia Colorectal Cancer Consortium, which showed a protective effect for soy-food intake against breast and colorectal cancer. Consortia with Chinese populations have been very successful in securing funding. The collaboration for tobacco control includes the China-U.S. Smokefree Workplace Partnership; mobile health (mHealth) projects that test mHealth tools, such as text messaging for smoking cessation; and support for the Health Information National Trends Survey (HINTS) in China. Top DCCPS scientific priorities for future collaborations include exploring health disparities in risk and occurrence, establishing Asian survivorship cohorts, and translating risk predictors into interventions.

Division of Cancer Epidemiology and Genetics. Dr. Chanock introduced an overview of DCEG studies in China, of which DCEG has more than 25 ongoing. DCEG has had more than 30 years of collaboration with China, including developing cancer maps that led to epidemiologic field studies and studying occupational exposures that were important in determining the carcinogenicity of chemicals. DCEG-Chinese collaborations are ongoing in many Chinese cities, and a large number of different academics have been trained and worked closely with DCEG. Special exposures studied in China have included occupational exposures to benzene, formaldehyde, trichloroethylene, and particulates, as well as the effects of physical activity. Observational studies, including studies of lung cancer in never-smoking women and people exposed to radon from living in underground dwellings, have the potential to lead to public health measures to decrease risk. The consortium to study the environmental and genetic etiology of lung cancer in never-smoking females has led to the identification of novel signals unique to non-smokers and linked residential histories to air pollution databases and satellite data. The ability to work closely with Chinese colleagues resulted in an individual exchange of data from GWAS of esophageal squamous carcinoma, the analysis of which led to the discovery of new susceptibility loci.

Dr. Abnet provided a review of DCEG studies in China of upper gastrointestinal (UGI) cancers. Eighty percent of the worldwide mortality from esophageal cancer is from squamous carcinomas, and half of those cancers occur in China. In 1985, a clinical trial of 30,000 Chinese farmers was sponsored by the NCI and NSFC to study UGI cancer. DCEG studies of UGI cancers in China include nutrition intervention trials for esophageal cancer, a *Helicobacter pylori* treatment trial for the prevention of gastric cancer, GWAS of esophageal and gastric cancer, and the effects of tooth loss and oral hygiene on the microbiome of the sputum and lung cancer risk. In the nutrition intervention trials, supplementation with a combination of vitamins and minerals, with selenium being the active agent, was found to reduce UGI risk, which had an incidence rate of approximately 20 percent. Early detection of esophageal lesions is key in successful intervention. Endoscopic localization with Lugol's solution was found to be highly specific for moderate and severe dysplasia, which has a high risk of conversion to tumors. A screening program was developed that was composed of identification of precursor lesions; endoscopic localization; staging; and therapy, for which many options exist. Long-term followup of endoscopic screening showed that early detection and intervention resulted in a significant reduction in esophageal squamous-cell carcinoma mortality. Non-endoscopic screening methods are needed, however, and methylation arrays and chromosomal abnormalities have been shown to be predictive in biorepository samples.

Division of Cancer Prevention. Dr. Kramer surveyed three primary collaborations between DCP and China: the Cancer Screening Trial Feasibility Study, the China Early Detection Research Network (EDRN), and Chinese translation of the Physician Data Query (PDQ[®]) database. Primary collaborators

include the National Institute/Hospital of Chinese Academy of Medical Sciences (CICAMS) and National Cancer Center (NCC), as well as the NCI Office of Communications and Public Liaison for the Chinese translation of the PDQ database. For the China Cancer Screening Trial Feasibility Study, CICAMS was very interested in lung and colorectal cancer screening, including confirming the National Lung Screening Trial (NLST) in a Chinese urban population, particularly with regard to generalizability and because of a different spectrum of causative exposures. The design of the feasibility study was to recruit from three cities in China of high, middle, and low socioeconomic status and have three study arms. A memorandum of understanding for the study was signed in May 2013, and the study now has completed the baseline screening phase. Center recruitment has been completed, although a significantly lower proportion of eligible participants were randomized in the lower socioeconomic status city. Preliminary data show a wide variation in computerized tomography (CT) lung abnormality by screening center and a wide range in the rate of non-calcified nodules/masses detected. Regarding the China EDRN, CICAMS is interested in establishing an EDRN infrastructure. To this end, joint monthly U.S.-China conference calls have been held, a common informatics center is assisting in establishing China databases, and China has sent a visiting scientist to the NCI to learn about EDRN processes and studies. The Chinese translation of the PDQ database is intended to extend the reach of PDQ cancer information to Chinese-speaking health professionals. In its pilot phase, health professional summaries for six cancer types of highest public health interest in China have been translated, reviewed by content experts, and placed online as the initial effort toward constructing the full website.

Impact of NCI Research Collaboration From China's Perspective. Dr. Qiao informed members about the importance of the collaboration between the U.S. NCI and the China Center for Disease Control and Prevention (China CDC). China first began a collaboration with the NCI in 1982 with etiological case-control studies on esophageal, lung, stomach, and choriocarcinoma cancers. Following these studies were a collaboration on a nutrition intervention trial, on which followup has continued for more than 30 years, and many etiological studies. Other notable collaborations have included cytology and HPV DNA tests for cervical cancer and an endoscopy screening collaboration, which included a visit to China by then-President Bill Clinton. Because of the discomfort caused by balloon cytology, China, with assistance from the United States, developed an endoscopy screening method, which also was able to include people living in the countryside. Dr. Qiao also noted several NCI–China educational and training programs. The Cancer Prevention Academic Course, organized since 1986, has benefitted many young Chinese investigators, including Dr. Qiao himself. Others include the NIH Fogarty International Clinical Research Scholars and Fellows Program, the Fulbright Public Health Program, and Fogarty Global Health Fellows.

Collaboration between the U.S. NCI and China CDC has had a strong positive impact on the Chinese. In Linxian, China, where the early esophageal and lung cancer studies took place, a public health plan put forth by Chinese investigators has led to an increase in healthy nutrition and a reduction in mortality from common cancers and elderly diseases. Data from a long-term study in a community in which one-time endoscopic screenings were given has revealed a 29 percent decrease in cumulative incidence of esophageal cancer among the target population and a 34 percent reduction in cumulative mortality from esophageal cancer. Dr. Qiao explained that collaborating with the NCI also has taught the Chinese about procedures surrounding ethical issues. For example, China has modeled its Institutional Review Boards on NCI projects. He also recognized the NCI's impact on Chinese health policy and regulatory concerns. Roundtable discussions have been held on such issues as HPV vaccine implementation and comprehensive prevention of cervical cancer in China. Dr. Qiao shared that in 2012, China's hospital director signed an agreement with Dr. Harold Varmus, then-Director of the NCI, to ensure future U.S. NCI–China CDC collaborations. Efforts will include the National Cervical Cancer Prevention Plan and Strategies, the Need for National Commitments to Cancer Research to Guide Public Health Investment and Practice, and the NCI Summer Curriculum in Cancer Prevention in China.

Dr. Y. Wang provided additional context for the NCI–China CDC collaboration, explaining that nearly 24 percent of deaths in China are caused by cancer, with especially high levels of lung, liver, and stomach cancers. The World Health Organization recommends tobacco control, physical exercise, and healthy nutrition to assist with cancer prevention, and China has taken steps in these directions. China also has engaged in a cancer screening project and increased its use of vaccines for cancer prevention. For example, an increase in hepatitis B vaccinations has reduced the incidence of liver cancer. Members were informed of a collaborative study begun with the NCI several decades ago on the occupational hazard benzene. The study helped researchers understand the biomarkers associated with benzene exposure and the biological effects at low exposure levels. The study also formed the basis of changing occupational threshold limits in China and has been used by the U.S. Environmental Protection Agency to reconsider its basis for allowable environmental levels.

Dr. Y. Wang elaborated on the long-term Chinese Children and Families Cohort Study (CFCS), a collaboration that began in 1993 as the Community Intervention Program of Folic Acid Supplements for Neural Tube Defect Prevention. The Program, which studied 240,000 pairs of mothers and offspring, showed that the prevalence of neural tube birth defects was reduced significantly when mothers were given folic acid supplements periconceptionally. This study informed the policy of folic acid supplements in China. Recently three pilot studies, including two related to cancers, were completed on a fraction of the CFCS families, and in progress is a feasibility study to determine whether CFCS families can be re-identified on a substantially larger scale.

Dr. Y. Wang expressed appreciation to the NCI for its ongoing collaboration with China on cancer research. He stated that areas for future collaboration include expanding research on the association of early life exposures and chronic diseases, such as cancer; strengthening cooperation, communication, and training on data collection and management, as well as on analysis of descriptive and analytic studies between the United States and China; continuing expansion and cooperation in the field on the study of cancer risk factors; and enhancing research and collaboration on cancer prevention, intervention, and vaccine development and application.

Discussion. Dr. Olopade thanked the CGH for providing focused information on cancer research efforts in China to the NCAB Subcommittee on Global Cancer Research and asked about similarities between patterns of cancer found in China and those of Asian immigrants living in the United States. Dr. Wang pointed out that an emphasis on tumor subtypes allows a more global comparison of commonalities or uniqueness. He added that because of significant heterogeneity in genomic and phenotypic levels, both functional and genomic studies are needed to determine targetable drivers and advance precision medicine.

Dr. Ley queried about the NCI's total investment supporting collaborative research in China, the percentage allocated to intramural versus extramural studies, and other NIH collaborative activities with China. Dr. Kramer responded that partnerships and country visits between the DCP and China focus on the PDQ[®] database and screening centers. Dr. Trimble indicated that NIAID; the National Heart, Lung, and Blood Institute (NHLBI); and the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development (NICHD) have collaborations with China. Dr. Qiao described one form of collaboration with American medical students in China receiving support for living expenses from a U.S. organization, such as Fogarty, and utilizing Chinese training facilities.

Dr. Marcia R. Cruz-Correa asked whether a past RFA on investment for low technology received applications regarding endoscopic screening. Dr. Trimble responded that no fundable applications for esophageal cancer were received in the first round of funding, but a project concerning the early diagnosis of hepatitis C infection was funded.

XI. ADJOURNMENT—DR. TYLER E. JACKS

There being no further business, the 5th joint meeting of the BSA/NCAB was adjourned at 4:30 p.m. on Wednesday, 24 June 2015.

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)(4), 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).

*The NCAB **en bloc** vote for concurrence with IRG recommendations was unanimous. During the closed session, a total of 2,769 NCI applications requesting direct cost support of \$915,636,681 and 14 FDA applications were reviewed.*

XIII. ADJOURNMENT—DR. TYLER E. JACKS

There being no further business, the Closed Session meeting of the NCAB was adjourned at 5:30 p.m. on Wednesday, 24 June 2015.

Date

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

Date

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