

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
167th NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
September 7, 2016**

**Conference Room TE406, East Wing, Shady Grove Campus
National Cancer Institute
National Institutes of Health
Bethesda, Maryland**

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
September 7, 2016

The National Cancer Advisory Board (NCAB) convened for its 167th regular meeting on 7 September 2016, in Conference Room TE406, East Wing, Shady Grove Campus, National Institutes of Health (NIH), Bethesda, Maryland. The meeting was open to the public on Wednesday, 7 September 2016, from 9:00 a.m. to 12:00 p.m. and 1:00 p.m. to 3:00 p.m., and closed to the public from 3:00 p.m. to 4:15 p.m. The NCAB Chair, Dr. Elizabeth M. Jaffee, Deputy Director, The Sidney Kimmel Comprehensive Cancer Center, Co-Director, Skip Viragh Center for Pancreas Cancer, The Dana and Albert “Cubby” Broccoli Professor of Oncology, Johns Hopkins University, presided during both the open and closed sessions.

NCAB Members

Dr. Elizabeth M. Jaffee (Chair)
Dr. Peter C. Adamson
Dr. Francis Ali-Osman
Dr. Deborah Watkins Bruner
Dr. Yuan Chang
Dr. David C. Christiani (absent)
Dr. Kevin J. Cullen
Dr. Judy E. Garber
Mr. Lawrence O. Gostin
Dr. Scott W. Hiebert
Dr. Beth Y. Karlan
Dr. Timothy J. Ley
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Mack Roach, III
Dr. Charles L. Sawyers
Dr. Margaret R. Spitz
Dr. Max S. Wicha

Alternate *Ex Officio* NCAB Members

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

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. 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. William Dahut, Acting Scientific Director for Clinical Research, Center for Cancer Research
 Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
 Dr. Paulette S. Gray, Director, Division of Extramural Activities
 Dr. Toby Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
 Dr. Warren Kibbe, Acting Deputy Director and 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. Dinah Singer, Acting Deputy Director and Director, Division of Cancer Biology
 Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
 Dr. Louis M. 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 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
 Ms. Paula Bowen, Kidney Cancer Association
 Mr. William Bro, Kidney Cancer Association
 Dr. Carol Brown, Society of Gynecologic Oncologists
 Dr. Margaret Foti, American Association for Cancer Research
 Dr. Leo Giambaresi, American Urological Association
 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. Shelley Fuld Nasso, NCI Council of Research Advocates
 Ms. Leah Ralph, Association of Community Cancer Centers
 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, SEPTEMBER 7, 2016**I. CALL TO ORDER AND OPENING REMARKS—DR. ELIZABETH M. JAFFEE**

Dr. Elizabeth M. Jaffee called to order the 167th NCAB meeting. Dr. Jaffee welcomed members of the Board, *ex officio* members of the Board, the President’s Cancer Panel (PCP), 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. Jaffee reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Dr. Jaffee welcomed the new NCAB members: Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology, Professor of Surgery, Professor of Pathology, Duke University Medical Center; Mr. Lawrence O. Gostin, University Professor, Faculty Director, Founding Linda D. and Timothy J. O’Neill Professor in Global Health Law, O’Neill Institute for National and Global Health, Georgetown University; Dr. Scott W. Hiebert, Hortense B. Ingram Chair in Cancer Research, Professor of Biochemistry, Department of Biochemistry, Vanderbilt University School of Medicine; Dr. Electra Paskett, Marion N. Rowley Professor of Cancer Research, Director, Division of Cancer Prevention and Control, Department of Internal Medicine, College of Medicine, The Ohio State University; Dr. Nancy J. Raab-Traub, Professor, Department of Microbiology and Immunology, School of Medicine, Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill; and Dr. Margaret R. Spitz, Professor, Dan L. Duncan Cancer Center, Baylor College of Medicine.

Motion. A motion to approve the minutes of the 21 June 2016 Joint Boards meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. ELIZABETH M. JAFFEE

Dr. Jaffee called Board members’ attention to future meeting dates listed on the agenda.

Motion. A motion to approve future NCAB meeting dates through 2018 was approved unanimously.

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

Dr. Douglas R. Lowy, Acting Director, NCI, welcomed new and continuing members of the Board and congratulated Dr. Jaffee on her new role as Chair of the NCAB. Dr. Lowy stated that one highlight of today’s meeting would be the report from the Blue Ribbon Panel on the Vice President’s Cancer Moonshot Initiative and conveyed NCI’s continued support of and commitment to other meritorious aspects of cancer research involving new and ongoing initiatives. Dr. Lowy provided an update on some of these initiatives, including investigator-initiated research, the Precision Medicine Initiative in Oncology (PMI-O), and cancer health disparities. He was joined by Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, who provided an update on the NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) trial and the NCI Virtual Drug Formulary.

Investigator-Initiated Research: Research Project Grant (RPG) Pool. Dr. Lowy informed members of a 25 percent increase in investigator-initiated awards from fiscal year (FY) 2013 to FY 2015 as reflected by the RPG pool; this is an increase from \$400 million (M) to \$500 M per year in new (Type 1) and competing (Type 2) awards. He stated that maintaining this award rate will require adding a total of \$300 M to the RPG pool from FY 2016 to FY 2022, which will necessitate adding

approximately \$80 M in FY 2017. Increased appropriations for the NCI will enable increases in funding to the RPG pool. Dr. Lowy remarked briefly on the 2-year decrease in the Program Project Grants being awarded and stated that the NCI is addressing this decrease by encouraging members of the extramural community to look more closely at applying for funding through this mechanism. The NCI endeavors to increase its overall investment in Program Project grants.

Precision Medicine Initiative in Oncology (PMI-O). Dr. Lowy reminded members of the goals of the President's PMI-O to improve cancer treatment through genomics by the development of genomic-based clinical trials; develop preclinical models to advance predictive oncology for targeted therapies; and develop a Genomic Data Commons (GDC), a large annotated database of cancer patients. He stated that the NCI had awarded several Administrative Supplements to existing grants (e.g., Cancer Center Support Grants, P50s, and U01/U10 grantees) since the initial PMI-O funding, including 18 awards to improve preclinical models for evaluating targeted therapeutics and immunotherapy; 25 awards to expand support for development of immunotherapy trials; and 10 awards thus far to employ clinical materials from drug-resistant patients for molecular analysis, which also will include additional awards to NCI Community Oncology Research Program (NCORP) sites for developing a repository on molecularly analyzed samples of resistant disease. Dr. Lowy stated that the NCI also is working to issue new Request for Applications (RFAs) to address these important issues.

Cancer Health Disparities. Dr. Lowy stated that the NCI is focusing on specific cancers (e.g., colorectal, liver, breast, prostate, multiple myeloma, and kidney cancers) that have associated health disparities to identify risk factors and the relative contributions of these risk factors to the disparities and to explore efforts to mitigate these risk factors. He described reports on health disparities associated with multiple myeloma and kidney and renal pelvis cancer. Incidence data from NCI's Surveillance, Epidemiology, and End Results (SEER) Program from 1992 to 2013 and mortality data on myeloma from the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) show that the incidence and mortality rates for African Americans are two times higher than other ethnic groups—the molecular understanding of what accounts for these differences is yet to be determined. In addition, incidence data from SEER and mortality data from NCHS on kidney disease show that incidence and mortality rates were higher in Native Americans despite the advances in molecular and genetic analysis of kidney cancer over the past 20 years. Molecular knowledge of kidney cancer in Native Americans is virtually unknown, and the NCI is sponsoring a research summit with Tribes in November 2016 in Oklahoma City, Oklahoma, to address these issues.

Dr. Lowy remarked on NCI's commitment to addressing cancer health disparities and described two research initiatives that evolved from the November 2015 meeting on health disparities. The Early Onset Malignancy Initiative, organized through NCORP, will develop the first minority-based cancer tissue bank of early-onset tumors and will collect information on treatment, response, and outcome. The other initiative is to develop new cancer models from tumors of minority patients; the Center to Reduce Cancer Health Disparities has already issued Research Supplements to begin these efforts. He stated that the NCI is making every effort to represent minorities appropriately in its clinical and preclinical research and are developing both cell- and animal-based models (e.g., cell lines, patient-derived xenografts, and 3-dimensional human tissue culture models) to advance cancer health disparity research.

NCI-MATCH Trial. Dr. Doroshow told members that following the May 31, 2016, reopening of the NCI-MATCH trial, the trial averaged 115 to 120 patient enrollments each week, which equated to 1,250 total accruals from June 2016 through August 2016. One-third of accruals were from NCI-designated Cancer Centers and two-thirds came from NCORP. He pointed out that the capacity for conducting genomic analysis and processing of initial biopsies had been expanded with the addition of new laboratories; the median time from receipt of material to results reporting was reduced to 13 days for 1,200 patients. The MATCH rate for the 23 open clinical trials is 25 percent. Also, five of the

23 trials will achieve their accrual goals soon and will be closing. Dr. Doroshow remarked on the 10 new treatment arms currently being evaluated and the potential for increasing patient enrollment to 7,000, which will enable completing accruals of patients with rare mutations. He pointed out that PMI-O funding is supporting detailed genomic analysis of all patients' samples, including next-generation, whole-exome, and RNA sequencing.

NCI Virtual Drug Formulary. Dr. Doroshow detailed the NCI Virtual Drug Formulary (Formulary) initiative. The Institute met with representatives from more than 20 pharmaceutical and biotechnology companies at the 2016 American Society of Clinical Oncology (ASCO) meeting to discuss streamlining the process for enabling Cancer Center investigators easier access to drugs for clinical trials. Several major companies expressed strong interest in the Formulary and the NCI has received pledges for 40 therapy drugs from 10 different companies; the next steps will be to renegotiate the current Cooperative Research and Development Agreements (CRADAs) with those companies. Investigators will submit proposals to the NCI that will be forwarded to the partnering companies, and evaluations should be completed within 8 weeks of the request. The NCI anticipates completing CRADA negotiations by late fall of 2016 and has begun to develop a website for the Formulary.

Questions and Answers

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, queried about the 10 new treatment arms being added, new companies joining the MATCH trial, and U.S. Food and Drug Administration (FDA) approved and unapproved drugs for the Formulary. Dr. Doroshow explained that many of the targets have backup compounds from different companies that will be activated after the initial trial is completed and may not represent new companies participating in the MATCH trial, although a range of companies have expressed interest in participating. As per current agreements, the Formulary will accept FDA-approved drugs and Phase II agents (that have completed safety and efficacy data) that are not approved.

Dr. Judy E. Garber, Director, Center for Cancer Genetics and Prevention, Dana-Farber Cancer Institute, Professor of Medicine, Harvard Medical School, congratulated the NCI on the success of the MATCH trial and asked about accrual distribution, expectations, and the second phase for the trials. Dr. Doroshow replied that five of the 23 active trials had achieved more than 50 percent accrual and an additional five trials are at 25 percent accrual. The studies that have achieved 50 percent accruals will be carefully evaluated, and decisions will be made to continue the course to 100 percent accrual or revert to using a backup target drug.

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, asked about plans for elucidating mechanisms of drug resistance and linking them to the biopsy data from drug-resistant patients enrolled in the MATCH trials. Dr. Doroshow stated that the NCI is very interested in obtaining these types of biopsies and that funds are available to support them. However, it will be up to the individual investigators to make these decisions.

Dr. Peter Adamson, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia, asked about the number of programs within the PMI-O that focused on childhood cancers. Dr. Doroshow replied that this information was not readily available but could be obtained.

In response to a query by Dr. Sawyers, Dr. Lowy clarified that the amount of funding had increased during the period before FY 2016 when there was a 3 percent increase in NCI's budget and the

average number of grants funded increased from 1,050 to 1,200 awards. The awards include a mixture of new and established investigators. Although the NCI is funding more applications, the successful application rate remains unchanged.

Dr. Barbara K. Rimer, Dean, Gillings School of Global Public Health, Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, expressed appreciation for the focus on health disparities and cautioned that patients identifying as multiracial (in the registry) would be challenging for the NCI to address. Dr. Lowy stated that one strategy would be to assign patients according to their genetic information when conducting genomic analyses and noted that Dr. Lynn Penberthy, Associate Director, Surveillance Research Program, Division of Cancer Control and Population Sciences (DCCPS), NCI, and her staff routinely reconcile these types of issues within the SEER Program.

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

Dr. Rimer reminded members of the mission of the President’s Cancer Panel (PCP, the Panel) to oversee the National Cancer Programs and report directly to the President on any barriers to the progress of those programs. Its main focus is to be assertive in areas where differences can be achieved and make actionable recommendations in those areas. She recognized two other members of the Panel: Mr. Hill Harper, cancer survivor, actor, and lawyer; and Dr. Owen N. Witte, Clinical Scientist, University of California at Los Angeles. Dr. Rimer expressed appreciation to PCP staff: Dr. Abby B. Sandler, Executive Secretary; Ms. Rachael Hanisch, Cancer Program Manager; and Ms. Lisa Paradis, Research Analyst. She also expressed appreciation to Senior DCCPS Fellow, Dr. Jennifer Moss, NCI staff, contractor services, and staff within other NIH Divisions.

Dr. Rimer remarked on the continued influence that the 2012–2013 report “Accelerating Human Papillomavirus (HPV) Vaccine Uptake: Urgency for Action to Prevent Cancer” has had and summarized some of the responses. The National Commission on Quality Measures for Healthcare Effectiveness Data and Information Set (HEDIS) for 2017 updated its adolescent immunizations to include HPV vaccination for both males and females, which will be reported in a single measure along with other adolescent vaccines (e.g., meningococcal and tetanus-diphtheria). The 69 Cancer Centers released a statement urging greater uptake of HPV vaccination for cancer prevention, and the 2016 HPV Summit brought together national leaders and representatives from the NCI, CDC, the Cancer Centers, and the American Cancer Society to discuss strategies for improving HPV vaccine uptake. In addition, ASCO released a statement urging aggressive efforts to increase HPV vaccination to prevent HPV-related cancers, the National HPV Vaccination Roundtable established in 2014 convened its second meeting in August 2016, and CDC’s Advisory Committee on Immunization Practices (ACIP) is reviewing evidence for a two-dose schedule with a 9-valent HPV (9vHPV) vaccine.

Members were informed that the content for the report on the 2014–2015 Panel series on “Improving Cancer-Related Outcomes with Connected Health” is being finalized, reviewed externally by multiple partners (e.g., NCI, ASCO, and CDC), receiving feedback from the White House liaison, and is expected to be released soon. Dr. Rimer recognized series Co-Chairs Drs. David Ahern and Bradford Hesse, both with DCCPS, who have been essential to the progress of the report and Dr. Warren Kibbe, Acting Deputy Director, NCI, for his input. She pointed out that the Panel will make its recommendations on topic areas important to Connected Health that include enabling development of tools to support individual’s health management and providers’ provision of care; encouraging the flow of health information among institutions, patients, and care providers; and strengthening the health information technology infrastructure.

The PCP's 2016–2017 series addresses “Ensuring Patients Access to High-Value Cancer Drugs.” The first workshop in this series, entitled “Access to and Cost of Cancer Drugs in a Changing Health Care Landscape,” was held June 2016 in New York City. The workshop focused on the following key areas: how innovations in therapy could transform treatment; increasing difficulties for some patients to access necessary drugs; and challenges created by rising drug costs and access for patients, providers, health care systems and payers. She pointed out that the series will examine factors influencing drug cost and pricing; use of rational pricing models; rising prices of cancer therapies; and streamlining clinical development processes. Participants included series Co-Chair Dr. Gary Gilliland, Director, Fred Hutchinson Cancer Research Center; Division Liaison Dr. Ann Geiger, Acting Associate Director, Healthcare Delivery Research Program, DCCPS; and representatives from diverse expertise and perspectives, including oncologists and oncology organizations, patient and patient advocacy groups, pharmaceutical and biotechnology companies, health economists, academic researchers, payers, and Federal agencies. Three more workshops are planned: “Emerging Opportunities to Streamline Cancer Drug Development” (December 2016 in Arlington, Virginia), “Rational Pricing Models” (March 2017, location to be determined), and “Rational Payment Models” (summer 2017, location to be determined).

Questions and Answers

Dr. Lowy stated that the PCP's report on HPV vaccine uptake has had an enormous effect on the community; vaccination rates for the last year, especially among boys, have been substantially higher. He added that Connected Health extends further than these topic areas to the issues of underrepresented minorities regarding rural health. Much of Connected Health is dependent on having access to devices such as smartphones, as confirmed by many investigators at academic institutions. Dr. Rimer explained that access to smartphone technology remains a problem in this country for millions of people due to affordability. Dr. Hesse noted NCI's increased efforts with other agencies, including the Federal Communications Commission (FCC), to address these issues of access and called attention to the soon-to-be-published data from NCI's Health Information National Survey, which has tracked rural access.

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, wondered how the connectivity issues that exist within the states that have low literacy rates were being addressed. Dr. Rimer recognizes that states with low literacy rates are of concern and pointed out that the report on Connected Health comments on making information available in ways that are culturally appropriate.

Dr. Beth Y. Karlan, Director, Women's Cancer Program, Samuel Oschin Comprehensive Cancer Institute, Director of Gynecologic Oncology, Department of Obstetrics and Gynecology, Cedar-Sinai Medical Center, and Professor, Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles, lauded the PCP's report on HPV vaccination for promoting change to policies and practices (e.g., ACIP's general recommendations), especially for middle schoolers, noting that 86 percent of students entering school have been vaccinated against HPV.

Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenebaum Cancer Center, and Professor of Medicine, University of Maryland, suggested updating the structure of future PCP reports on Accelerating Human Papillomavirus (HPV) Vaccine Uptake to accommodate the changing guidelines and vaccine availability.

Dr. Lowy strongly emphasized the need to approach the questions around access to and cost of cancer drugs in a balanced and scientific manner; he looks forward to a report that illuminates how to deal with this enormously complex, but critically important issue. Cancer, as others have stated, is one of

the most common causes of bankruptcy; patients often face having to choose between buying their medications and paying their mortgage.

In response to a query from Dr. Sawyers, Dr. Sandler explained that pharmaceutical company representatives are engaged in the discussions on drug costs and attendance at the first workshop. Efforts are ongoing to increase their participation. The PCP welcomes input from the members on companies to engage.

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

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations (OGCR), reported on the final weeks of the 114th Congress, the status of the Congressional appropriations, and legislation of interest. She stated that FY 2016 ends in 23 days, which more than likely means that the NIH and NCI will operate under a Continuing Resolution (CR) well into FY 2017; the Senate and House appropriations committees are debating the duration of the CR. The possibilities being debated are September 2016 to mid-December 2016, favored by the committees and leadership; September 2016 to mid-March 2017, favored by the House Freedom Caucus; and post-election options for an Omnibus appropriations bill for FY 2017, CR into March 2017, or a full-year CR. Congress has until September 30, 2016, to avoid a government shutdown.

The Senate passed a bill to increase funding to the NIH by \$2 B and to the NCI by \$216 M; the House passed a bill to increase funding to the NIH by \$1.25 B and to the NCI by \$124 M. The committees declined to cut \$1 B in discretionary funding for the NIH. The FY 2018 budget process will begin in the spring of 2017 with the new President's budget request. Bipartisan support for the NIH and the NCI remains strong. The Senate appropriations committee strongly supports the goals of the Cancer Moonshot Initiative and looks forward to the spending details once the Federal Task Force (Task Force) presents its report.

Questions and Answers

Dr. Lowy reminded members that Ms. Holohan and OGCR are available to discuss other legislative issues that the Board is interested in and that their services are not limited to those reported on at this meeting. Ms. Holohan added that her office works closely with government relations teams at universities and professional associations to educate Congress on opportunities in cancer research.

VI. CANCER MOONSHOT BLUE RIBBON PANEL (BRP) REPORT—DRS. TYLER E. JACKS, ELIZABETH M. JAFFEE, AND DINAH SINGER

Overview of the NCI Cancer Moonshot and the BRP. Dr. Tyler Jacks, Director, Koch Institute for Integrative Cancer Research, David H. Koch Professor of Biology, Massachusetts Institute of Technology, expressed appreciation to the BRP, the Co-Chairs, and members of the Working Groups for their tireless efforts. He also expressed appreciation to the NCI staff who assisted the BRP in its activities and applauded Dr. Dinah Singer, Acting Deputy Director, NCI, who has devoted the majority of her time during the past 5 months to the Cancer Moonshot Initiative.

Dr. Jacks began by providing members the overall perspective of the BRP and the processes that have led to the Report of the Cancer Moonshot (Report). The Cancer Moonshot was announced during President Obama's January 2016 State of the Union Address. The goals of the Cancer Moonshot are to accelerate progress in cancer, including prevention and screening; encourage greater cooperation and collaboration within and between academia, government, and the private sector; and enhance data sharing. The President tasked Vice President Joseph Biden with organizing and overseeing this effort;

the Vice President and his office convened the Task Force, which comprises heads of the executive branch departments, agencies, and offices in the Federal Government.

The Task Force charged the NCAB and the NCI to establish a BRP to provide scientific input and make specific recommendations regarding what work should be done. The NCAB then established the BRP (led by three Co-Chairs) who in turn organized seven Working Groups to assess the science in key areas and to develop recommendations for the Cancer Moonshot; the report of this work is being presented at today's meeting. After approval, this report will be forwarded to the NCI and the Task Force. In addition to addressing the charges to broadly accelerate the community's understanding of cancer—its prevention, early detection, treatment, and cure—and improve access to new research, data, and care, the Task Force examined non-science issues. Specifically, the Task Force identified regulatory barriers or challenges that exist among Federal agencies that could be overcome to improve the efficiency of cancer research and the implementations of new scientific discoveries for the benefit of the patients.

Dr. Jacks stated that through its Working Groups, panels of experts from cross-cutting disciplines, the BRP chose those areas of science that through increased funding and organizational structures could be accelerated (to achieve in 5 years what would otherwise take 10 years) for rapid benefit of the patient. He recognized the members of the BRP, the Working Groups and their affiliations; members of NCAB and Board of Scientific Advisors (BSA), and representatives from patient advocacy groups and industry who participated in the Cancer Moonshot Initiative. Including NCI staff, a total of 150 people labored diligently and audaciously in the work of the BRP, attending many WebEx meetings and conferences. The Working Groups concentrated on opportunities in seven areas: Cancer Immunology, Clinical Trials, Enhanced Data Sharing, Implementation Science, Pediatric Cancer, Precision Prevention and Early Detection, and Tumor Evolution. In addition to the internal workings of the BRP, the NCI established scientific and community outreach activities (e.g., online public repository, one-on-one input via emails, BRP listening sessions, and professional organizations) to provide ideas and suggestions.

The Working Groups submitted 14 recommendations to the BRP; 13 were approved as Moonshot recommendations, and one was converted to a demonstration project. Of the 13 approved, three with cross-cutting themes were combined into single recommendations, without loss of impact or significance, bringing the total recommendations for the Cancer Moonshot to 10. These 10 are provided in the Report and the 13 original recommendations are available on NCI's website: www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel. The cross-cutting themes include development of a national network of patient biological and clinical data; prevention and health disparities research; biomarkers; development of technology and preclinical models; data sharing, analytics, and predictive computational modeling; and collaborations of public-private partnerships.

Summary of the Recommendations. Dr. Jaffee outlined the 10 scientific recommendations and described the Moonshot ideas of each. She emphasized that the recommendations are all are of equal importance and were not ordered in the report according to priority.

- A. **Network for Direct Patient Engagement.** Enlist patients in a federated network where they can “pre-register” for clinical trials and contribute their tumor profile data to expand knowledge about what therapies work, in whom, and in which types of cancers.
- B. **Cancer Immunotherapy Clinical Trials Network.** Organize a network to discover and evaluate novel immune-based approaches for adult and pediatric cancers and eventually develop vaccines to prevent cancers of all types.

- C. **Therapeutic Target Identification to Overcome Drug Resistance.** Launch interdisciplinary studies to delineate mechanisms that lead cancer cells to become resistant to previously effective treatments, with the goal of informing the development and clinical testing of new therapies.
- D. **A National Cancer Data Ecosystem for Sharing and Analysis.** Form a national infrastructure for sharing and processing cancer data by developing an ecosystem to collect, share, and interconnect data sets.
- E. **Fusion Oncoproteins in Pediatric Cancer.** Improve understanding of the abnormal fusion proteins that result from chromosomal translocations that drive many pediatric cancers and eventually develop therapeutic approaches that target these mechanisms.
- F. **Symptom Management Research.** Support research to accelerate the development of guidelines for management of patient-reported symptoms to improve quality of life and adherence to treatment regimens.
- G. **Prevention and Early Detection: Implementation of Evidence-Based Approaches.** Conduct implementation science research to encourage broader adoption of HPV vaccination, colorectal cancer screening, and tobacco cessation.
- H. **Retrospective Analysis of Biospecimens From Patients Treated With Standard of Care.** Analyze archival tumor samples from cancer patients treated with standard-of-care therapies to learn which features predict outcome to better plan treatment for future patients.
- I. **Generation of Human Tumor Atlases.** Catalog the evolution of genetic lesions and cellular interactions in tumor/immune/other cells in the tumor microenvironment, from the earliest detected lesions to metastasis for both adult and pediatric cancers.
- J. **Development of New Enabling Cancer Technologies.** Support development of technologies to accelerate testing of therapies and tumor characterization.

Dr. Jaffee then summarized the three proposed demonstration projects. These projects are parts of the prevention, immunotherapy, and emergent technologies recommendations that can be executed more rapidly. The Prevention and Early Detection Lynch Syndrome (LS) demonstration project is a national effort to systematically screen all colorectal and endometrial cancer patients for LS. First-degree relatives of patients with LS would be given the options of being screened or receiving genetic counseling. The Pediatric Cancer Immunotherapy Network demonstration project proposes to develop a national pediatric immunotherapy clinical trials network to facilitate the testing of new immunotherapy approaches in childhood cancers. This network will help to establish a robust research pipeline to advance pediatric immunotherapy. The Tumor Pharmacotyping demonstration project will develop intra- and extra-tumoral technologies for determining the most effective therapeutic agents for individual patients.

Next Steps. Dr. Singer expressed appreciation to the BRP Co-Chairs, Drs. Jaffee and Jacks, the BRP members, Working Groups Co-Chairs and members for their enduring efforts during the past 5 months. The delivery to the NCAB of the BRP Report on those recommendations of research that could be accelerated through the additional support and funding of the Cancer Moonshot completes one phase of the Cancer Moonshot Initiative; the next phase will be adoption and implementation of the

proposed recommendations. This Report will then be transmitted from the NCAB to the NCI Director, who will forward it to the Task Force. The recommendations set forth from the NCAB will advise the NCI on the future directions and programs that relate to the Cancer Moonshot. Policy issues identified by the BRP as barriers to doing the work already have been forwarded to the Task Force. Implementation of the recommendations (clinical and patient-centered) will depend on the extent to which these barriers are addressed.

The NCI will consider the following approaches for implementing the recommendations: identify those recommendations that are most feasible to implement in FY 2017; leverage ongoing or planned NCI initiatives that will advance the goals of the recommendations; consider new funding mechanisms (e.g., Other Transaction Authority) other than grants and cooperative agreements to enable efficient and effective implementation; develop approaches to streamline existing mechanisms; and establish partnerships with other Federal agencies and public-private partnerships with industry leaders. The extent and rate of implementation will depend on Congressional appropriations; the NCI will rely on its advisory boards and the BRP for advice during the implementation process. Continued investment in investigator-initiated research and research areas beyond the scope of the BRP remains a high priority.

Questions and Answers

Members congratulated the BRP on a splendid report and for meeting the challenge to undertake an extraordinary amount of work to generate recommendations that could be accelerated for the Vice President's Cancer Moonshot. They expressed appreciation to the entire team that participated in the activities of the BRP and to the NCI and its leadership. This is a historic time in cancer research and the recommendations have great potential to be impactful and improve patient outcomes.

Dr. Cullen facilitated the question and answer session.

Dr. Ali-Osman asked about the rationale used in selecting the demonstration projects and the goals they hoped to achieve. Dr. Singer explained that the LS demonstration project was developed from the Precision Prevention and Early Detection (Prevention) Working Group as a way to identify people with genetic predispositions to cancer that could result in prevention, screening, and early detection. Dr. Jacks added that other demonstration projects (e.g., exploring emerging technologies and pediatric immunotherapies) represented ideas that did not meet the criteria for a Cancer Moonshot, but were potentially important projects to highlight that could be explored as demonstration projects.

Mr. Gostin asked about the role of primary prevention and its importance in the recommendations. Dr. Singer replied that the Prevention Working Group discussed a large number of areas to focus on and decided on genetic predispositions that affect more than 1 million people unawares. The Implementation Science (IS) Working Group discussed a wide range of evidence-based interventions and decided to propose ones that were not currently being implemented. Dr. Paskett explained that the IS Working Group decided to focus on areas of proven success that could be addressed rapidly. Dr. Garber added that the Prevention Working Group attempted to identify in a demonstration project those studies that would make a difference to a large population with implications of new models for genetic testing and counseling and that were affordable and practical to implement. Dr. Jaffee echoed the practicality of developing recommendations that could be implemented in the short term as high priorities. Dr. Lowy stated that the recommendations were not limiting the areas that could be accelerated and that the NCI is supporting many other areas beyond these specific recommendations.

In response to a concern expressed by Dr. Wicha about potentially diverting resources from an area where they could be more useful by doing retrospective studies, Dr. Sawyers stated that the recommendation to build a network for direct patient engagement involves doing prospective studies of

patients on clinical trials and that the retrospective studies will leverage existing resources to address adjuvant therapy decision making. Dr. Singer added that NCI's implementation phase of the Cancer Moonshot would decide whether retrospective or prospective studies best suited the recommendations.

Dr. Paskett suggested including relevant statistical information for all of the recommendations and statements on population science and health disparities in the Report of the Cancer Moonshot. Dr. Spitz suggested placing more emphasis on the transformative potential of the recommendations in the Report as well.

In response to questions on the status of policy recommendations for the Cancer Moonshot Initiative, Mr. Greg Simon, Executive Secretary, Cancer Moonshot Federal Task Force, explained that the Task Force had been in discussion on these issues at its biweekly meetings; their deliberations will be included in the report that is due to be released in October 2016. He emphasized that the policy issues (e.g., lack of data sharing; increased diversity and training in the workforce; and outreach to underrepresented groups) brought forth were germane to the research culture but remain unresolved. These policy issues can be addressed through direct, Congressional, Presidential, or international action. The main focus has been to distinguish between ordinary and Moonshot ideas; preventive efforts, such as the LS demo project and improving the rate of HPV adoption, are true Moonshot issues. Other issues being considered at the Task Force level are health disparities, access to care (clinical cancer centers and community centers), access to clinical trials, and geographic disparities in survivorship, and opportunities for standard care. Mr. Simon commended the NCI and the BRP for being a breakthrough research panel that worked at enormous speed to generate quality recommendations. He relayed the Vice President's sentiments of gratitude for the creative and significant recommendations; the Vice President remains committed to ensuring that the recommendations are advanced forward.

In response to a query from Dr. Bruner, Dr. Jaffee replied that the immunotherapies clinical trials network would focus on targeted clinical trials to answer scientific questions in the patients that would be similar to the NCI-MATCH trials. Dr. Jacks added that the main objective is to bring together scientific oversight and coordination to use decision making tools to determine what drugs would be tested and how they would be tested and analyzed. The clinical trial design would leverage existing infrastructure, such as NCI's National Clinical Trials Network (NCTN).

In response to members' questions on the lack of appropriations for the Cancer Moonshot, Dr. Singer pointed out that the BRP was charged to identify the scientific opportunities and was not tasked with addressing the funding questions early on. The NCI is developing different implementation schema to address the issues of funding. Dr. Jacks added that Congressional funding and opportunities through public-private partnerships would play a key role. Dr. Lowy stated that the NCI is optimistic that the compelling set of recommendations will translate into increased appropriations for FY 2017. The Institute has no immediate plans to prioritize the recommendations, but will initially do what is feasible in implementation; there is an absolute need to increase NCI's funding to accelerate 10 years of progress to 5 years. He applauded the intervention and strong leadership of Vice President Biden and looks forward to the cancer community's partnering with the NCI to make new strides in cancer research.

Dr. Mack Roach, Professor of Radiation, Oncology, and Urology, and Chair, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, strongly recommended that the Report detail the burden of health disparities and articulate in a clear-cut manner how the recommendations will change these health disparities within 5 years. Strategies to reduce disparities in 5 years should be a priority; health disparities data have revealed for longer than 20 years that African Americans are 50 percent more likely to die from cancer. He pointed out that cooperative groups currently engaged in doing immunotherapy trials should not be considered outside the scope of the Moonshot; they should be integrated into traditional treatment.

Mr. Simon affirmed that health disparities were included in the discussions of the Task Force and that Vice President Biden was briefed on such disparities early on.

In response to members' questions about including today's comments in the final Report, Dr. Singer replied that the comments and suggestions would be incorporated before the Report is forwarded to the NCI. Members requested the opportunity to review the updated version of the document before it is submitted to the NCI.

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Washington University School of Medicine, asked about ways the Moonshot would incorporate the development of new targeted drugs into a working plan to engage the pharmaceutical industry and whether RFAs would be used for pilot projects. Dr. Jacks recognized new target drug opportunities as an important area and pointed out that the science being supported in the Generation of Human Tumor Atlases recommendations could lead to the discovery of new targets; these discoveries could lead to investigator-initiated activities and/or opportunities for the pharmaceutical industry. Dr. Singer added that the NCI is discussing several flexible and efficient funding mechanisms, and RFAs may be included.

Dr. Nancy J. Raab-Traub, Professor, Department of Microbiology and Immunology, School of Medicine, Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, expressed concern that the etiology of the initiation or progression of cancer was not addressed as a cross-cutting theme in the recommendations. Dr. Jacks explained that the etiology of cancer will be addressed in the Generation of Human Tumor Atlases recommendations and referred members to the full Working Group reports listed on NCI's website. Dr. Singer stated that the NCI will continue to support a portfolio of fundamental cancer biology activities, which will interface with and complement these recommendations.

In response to a query from Dr. Karlan on long-term toxicities of cancer and cancer therapies, Dr. Singer responded that individual toxicities were not specifically addressed, but primary, secondary, and survivorship issues were included in the recommendations.

In response to concerns expressed by Dr. Garber on compromising the other work that the NCI does, Mr. Simon replied that the work of the Task Force is to recommend new ways for traditional work to be performed and to improve efficiency; this will not preempt the other work that the NCI is doing.

Dr. Adamson recommended that the Board provide a bold and clear statement that an increase in sustained Congressional investment is necessary for the success of the Vice President's Cancer Moonshot Initiative and without such an investment the Initiative would fail. Dr. Roach added that members should continue to be vigilant in ensuring that the message is clear that medicine, science, and cancer research are moving away from doing business as usual.

Motion. A motion to accept the BRP's draft Report of the Cancer Moonshot was approved with the stipulation that the Report be updated to include NCAB member's comments. There was one abstention.

Motion. A motion to urge increased and sustained appropriations from Congress to support the Cancer Moonshot Recommendations was approved unanimously.

VII. NCI GENOMIC DATA COMMONS (GDC) STATUS—DR. WARREN KIBBE

Dr. Warren Kibbe reminded members that the GDC, an existing effort to standardize and simplify submission of genomic data to the NCI, is a part of the NIH Big Data to Knowledge (BD2K) Initiative and an example of the broader NIH Commons. Its operating principles of making data findable,

accessible, interoperable, and reusable (FAIR) overlap the BRP's recommendations and the Vice President's Cancer Moonshot goals on data sharing. The GDC went live on June 6, 2016, containing 14,500 submissions, most of which were from large-scale NCI programs, such as The Cancer Genome Atlas (TCGA), Therapeutically Applicable Research to Generate Effective Treatment (TARGET), the Cancer Genome Characterization Initiative, and the Cancer Cell Line Encyclopedia. The recent data sharing agreement between the NCI and Foundation Medicine, Inc. will add 18,000 genomic profiles to the GDC. In the next 1 to 3 years, the GDC will continue to increase the power and utility of its resources with submissions from the NCI-MATCH trials, Clinical Trial Sequencing Program, Cancer Driver Discovery Program, Human Cancer Model Initiative, and Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network. In addition, the GDC provides an interactive data portal and user interface to guide the user through the various disease sites and the types of submissions that are linked; data submissions by investigators; and the database of genotypes and phenotypes (dbGAP).

Dr. Kibbe pointed out that on a broader scale the GDC was developed to foster the molecular diagnosis and treatment of cancer and promote PMI-O by helping to build a National Cancer Knowledge System as envisioned in the 2011 National Academy of Medicine (formerly the Institute of Medicine) report entitled "Toward Precision Medicine." The infrastructure and functionality behind the GDC will accommodate open-access users, controlled-access users, and data submitters. Open-access users will have access only to open-access data. Controlled-access data and data submission are controlled through NIH's electronic Research Administration Commons and control access agreements in dbGAP. The GDC is an asset to the cancer community in its ability to store raw genomic data, utilize shared bioinformatics, and maintain harmonized clinical data. NCI's commitment to maintaining long-term storage of cancer genomic data in the GDC at no cost to the investigator and the researcher's ability to comply with the NIH Genomic Data Sharing policy are of major benefits as well.

The NCI also is supporting Cancer Genomics Cloud Pilots to provide a comprehensive infrastructure for cancer genomic data to computationally support the cancer community. The goals of the GDC and cloud pilots are to support the PMI; provide a data integration platform to allow multiple data types; work with the Global Alliance for Genomics and Health to define the next-generation secure, flexible, meaningful, interoperable, lightweight interfaces—that is, open application programming interfaces (APIs); and engage the cancer community in evaluating the open APIs for ease of use and effectiveness. The GDC and cloud pilots will help to form the larger cancer data ecosystem.

Questions and Answers

In response to a query by Dr. Sawyers on accepting data from other countries into the GDC, Dr. Kibbe explained the restrictions for accessing data from other countries and stated that proper agreements will need to be established. The APOLLO Network has data sharing agreements with Australia's Proteome of Human Cancer, under the Memorandum of Understanding agreements signed between the United States and Australia, and is a good system to leverage. The Data Model Advisory Group, an external advisory group for the GDC, has been focused on getting the system operational and now may shift its focus on other issues, such as recruitment of data. In response to Dr. Ley's query about addressing data submissions problems with dbGAP and ways to incorporate professional clinical annotations in the GDC, Dr. Kibbe replied that the GDC only uses dbGAP for registering projects; all data submissions occur directly with the GDC's components. Leveraging existing model databases involved in clinical annotation will be a good place to start addressing professional clinical annotations in the GDC.

Dr. Paskett recommended including more patient-reported data and patient-reported outcomes data in the GDC and asked about the data sharing engagement with underserved populations to ensure

diverse representation in the GDC. Dr. Kibbe explained that the GDC is equipped to handle patient-reported outcomes data and that similar data from other NIH initiatives have been submitted. The issue of diverse representation should always be at the forefront in research and must be built into experimental designs before data are collected.

VIII. CELLS AS DRUGS: NEXT-GENERATION CANCER IMMUNOTHERAPIES— DR. NICHOLAS P. RESTIFO

Dr. Nicholas P. Restifo, Senior Investigator, Surgery Branch, Center for Cancer Research (CCR), NCI, reported on his most recent insightful findings that describe how two fundamental elements, oxygen (⁸O) and potassium (¹⁹K), have an effect on cancer; these naturally occurring elements can be thought of as novel “elements” of immune suppression within the tumor microenvironment. At the center of successful cancer immunotherapies is the T lymphocyte (T cell), which provides the specificity that enables recognition of mutations that are expressed by tumor cells. Metastasis accounts for more than 90 percent of cancer deaths and it requires invasion from the immune system; the lung (highly oxygenated) is a common site of metastasis for many cancers. During the initiation and growth of a tumor, the tumor microenvironment changes; cells move from normal oxygen conditions (normoxic) to oxygen deficient conditions (hypoxic). Building on previous observations in his laboratory, Dr. Restifo hypothesized that site-specific environmental factors, such as oxygen, help establish immunologically permissive sites for metastasis.

T cells use the prolyl hydroxylase domain (PHD)-containing proteins to sense oxygen in the lungs and degrade hypoxia inducible factor in the presence of oxygen. The *Egln* gene, which encodes the PHD oxygen sensors, is located at three different sites in the human genome. Generating PHD triple knock-out (PHD-tKO) mice to study intrinsic oxygen sensing in T cells, Dr. Restifo’s laboratory was able to show that T-cell intrinsic PHD proteins suppress spontaneous pulmonary inflammation; cluster of differentiation (CD) 8⁺ and CD4⁺ cells that lack PHD proteins are prone to produce interferon gamma (IFN-γ) after stimulation; T-cell intrinsic expression of PHD proteins licenses tumor colonization in the lung, but not in subcutaneous tissue; and PHD proteins suppress type 1 responses against innocuous house dust mite antigen.

Dr. Restifo told members that adoptive cell transfer (ACT) was well developed at the NCI, mostly due to the work of Dr. Steven A. Rosenberg, Chief, Surgery Branch, CCR, and other cancer centers, including Memorial Sloan Kettering and the University of Pennsylvania, where they adoptively transfer tumor reactive T cells into patients with cancer. ACT can be curative in patients, but it needs to be developed further to gain FDA approval. Recognizing that oxygen sensing by T cells establishes an immunologically tolerant metastatic niche in the lungs and other well oxygenated sites, the Restifo group hypothesized that the inhibition of PHD proteins could improve ACT immunotherapy. To explore this hypothesis, the laboratory used the tyrosinase-related protein 1 T-cell receptor (TRP-1 TCR) transgenic system to model ACT, whereby antigen-specific TRP-1 CD4⁺ T cells are expanded *ex vivo* and transplanted into mice bearing established subcutaneous or pulmonary B16 melanoma tumors; PHD proteins were inhibited with dimethylxalyglycine (DMOG), a hydroxylase inhibitor. Findings showed that DMOG blocks the oxygen-sensing PHD proteins, as evidenced by RNA sequence and gene set enrichment analysis, and inhibition of PHD proteins with DMOG both changes the function and phenotype of T cells and improves ACT immunotherapy. In addition, similar maneuvers can be done with human CD4⁺ cells.

Dr. Restifo explained that tumors of patients treated at NCI’s CCR often exhibit tumor microenvironments that are characterized by a high density of necrosis, which has been correlated with poor prognosis and early death. As tumors change from normoxic to hypoxic conditions, the PHD

oxygen-sensing properties are decreased, cellular necrosis is increased, and intracellular ions, such as potassium [K⁺], are released into extracellular space. In collaboration with CCR surgeons Drs. W. Marston Linehan and David S. Schrupp, the Restifo group was able to show in freshly resected tumors that the interstitial fluid had elevated concentrations of extracellular [K⁺], which correlated with increased cell death (Eil et al., *Nature*, in press, Fall 2016). The Restifo laboratory further investigated whether elevated extracellular [K⁺] had an effect on T cells and showed that tumor interstitial fluid contained 40 millimoles (mM) of [K⁺]; elevated [K⁺] produces profound suppression of human and mouse TCR-induced effector function; hyperkalemia produces profound suppression of TCR-induced transcripts, including interleukin 2 (IL-2) and IFN- γ ; and tumor-associated hyperkalemia augments checkpoint inhibition of T cells that may already be in place. In addition, T cells can be genetically engineered for resistance to hyperkalemia by overexpressing the [K⁺] transporter, Kcan3, in anti-tumor T cells, and anti-tumor cells that overexpress Kcan3 have enhanced therapeutic efficacy.

In closing, Dr. Restifo pointed out that tumor-induced immunosuppression is complex, involving many biological and genetic processes. However, these findings offer basic approaches to tumor suppression and explored how ⁸O and ¹⁹K, two elements from the periodic table, can be used to destroy cancer. He acknowledged Dr. David Clever, a guest researcher in his laboratory, and Dr. Robert Eil, Clinical Fellow, currently at Oregon Health & Sciences University, for their contributions on this work. He also expressed appreciation to the CCR clinical team, the Rosenberg laboratory, and the many collaborators for their support.

Questions and Answers

Dr. Jaffee asked about the translational aspects of these studies and wondered if other oxygenated tissue, like the liver, that were sites of metastasis had been studied. Dr. Restifo replied that the responses they have observed, a quelling of immunity, is adaptive in healthy oxygenated tissues and might include the liver. Preliminary results reveal an oxygenation effect in a liver metastasis model that is being developed in collaboration with Dr. Tim Greten, NCI.

In response to a query from Dr. Raab-Traub about differences in tumor vascularization, Dr. Restifo explained that these are new findings and that experiments to measure tumor vascularization have not been done.

Dr. Karlan wondered if preventive measures were needed when doing surgery on well-oxygenated tumors. Dr. Restifo recognized the importance of knowing this and explained the difficulty in measuring the effect of oxygen during surgery and other interventions when air is moving into and out of the lungs (e.g., normal breathing).

Dr. Ali-Osman asked whether other cells in the microenvironment played a role in these findings. Dr. Restifo described what models the laboratory can use to study the effects of other cell types; these models can be shared with the cancer community.

In response to a query from Dr. Wicha about experiments to determine how the hypoxic environment affected the immune system, Dr. Restifo replied that in the absence of tumor necrosis, the findings showed that the immunosuppressive effects were augmented under hypoxic conditions.

IX. ONGOING AND NEW BUSINESS—DR. ELIZABETH M. JAFFEE

Subcommittee Meetings. Dr. Jaffee stated that no subcommittee meetings were held prior to today’s meeting. Assignments will be sent to the members with the expectation of convening those meetings prior to the Joint December 2016 Joint Board meeting.

Future Agenda Items. Dr. Roach suggested including presentations from the Cancer Moonshot Task Force regarding policy issues at the next meeting. He mentioned the issue of reimbursements for cancer treatment given outside of the United States and the lack of Centers for Medicare and Medicaid Services (CMS) authorizations. An opportunity exists to be involved in cooperative activities globally for treatments not available in the United States and to investigate extending CMS’ authority on payments.

Dr. Lowy stated that the report from the Task Force will be available at the December 2016 meeting, but discussions on policy issues are not limited to those submitted by the BRP.

X. CLOSED SESSION—DR. ELIZABETH M. JAFFEE

“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 Board was informed that a comprehensive listing of all grant applications to be included in the en bloc vote was in the Special Actions package. Those grant applications, as well as those announced during the closed session, could be considered for funding by the Institute.

The NCAB **en bloc** vote for concurrence with Initial Review Group (IRG) recommendations was unanimous. During the closed session, a total of 2,258 NCI applications were reviewed requesting direct cost support of \$752,543,783. Three FDA Small Business Innovation Research (SBIR) applications requesting direct cost support of \$752,366 also were included in the **en bloc** vote for concurrence.

XI. ADJOURNMENT— DR. ELIZABETH M. JAFFEE

Dr. Jaffee thanked all of the Board members, as well as all the visitors and observers, for attending.

There being no further business, the 167th regular meeting of the NCAB was adjourned at 4:15 p.m. on Wednesday, 7 September 2016.

Date

Elizabeth M. Jaffee, Ph.D., Chair

Date

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