

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

**11th JOINT MEETING
of the
BOARD OF SCIENTIFIC ADVISORS AND
NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
June 26–27, 2018**

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

**BOARD OF SCIENTIFIC ADVISORS and
NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
June 26–27, 2018**

The Board of Scientific Advisors (BSA) and the National Cancer Advisory Board (NCAB) convened for the 11th Joint Meeting on June 26–27, 2018, in Conference Room TE406, East Wing, Shady Grove Campus, National Cancer Institute (NCI), National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, June 26, 2018, from 8:30 a.m. to 3:45 p.m., and Wednesday, June 27, 2018, from 9:00 a.m. to 11:12 a.m., and closed to the public Tuesday, June 26, 2018, from 4:00 p.m. to 4:51 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, and on behalf of the BSA Chair, Dr. Chi V. Dang, Dr. Ethan M. Basch, Professor of Medicine, Division of Oncology, School of Medicine, Professor of Public Health, Department of Health Policy and Management, Gillings Global School of Public Health, Director, Cancer Outcomes Research Program, Co-Leader, Cancer Prevention and Controls Program, Lineberger Comprehensive Cancer Center, University of North Carolina (UNC) at Chapel Hill, presided during the open session. Dr. Jaffee presided during the closed session.

BSA Members

Dr. Chi V. Dang (Chair) (absent)
Dr. Kenneth C. Anderson (absent)
Dr. Dafna Bar-Sagi
Dr. Ethan M. Basch (Acting Chair)
Dr. Michael John Becich
Dr. Melissa L. Bondy (absent)
Dr. Arul M. Chinnaiyan (absent)
Dr. Graham A. Colditz
Dr. Christopher M. Counter
Dr. Karen M. Emmons
Dr. Carol E. Ferrans (absent)
Dr. James V. Lacey
Dr. Maria Elena Martinez
Dr. Luis F. Parada
Dr. Sylvia Katina Plevritis
Ms. Diane Zipursky Quale
Dr. Martine F. Roussel
Dr. Robert D. Schreiber (absent)
Dr. Victoria L. Seewaldt
Dr. Kevin M. Shannon
Ms. Mary L. Smith (absent)
Dr. Ian M. Thompson Jr.
Dr. David A. Tuveson (absent)
Dr. Cheryl L. Walker
Dr. Eileen P. White
Dr. Kevin P. White
Dr. Cheryl L. Willman

NCAB Members

Dr. Elizabeth M. Jaffee (Chair)
Dr. Peter C. Adamson (absent)
Dr. Francis Ali-Osman
Dr. Deborah Watkins Bruner
Dr. Yuan Chang (absent)
Dr. David C. Christiani
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 (absent)
Dr. Margaret R. Spitz (absent)
Dr. Max S. Wicha

Alternate *Ex Officio* NCAB Members

Dr. Robert T. Anderson, DOE (absent)
Dr. Michael A. Babich, CPSC (absent)
Dr. Vincent J. Cogliano, EPA
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS
Dr. Richard Pazdur, FDA (absent)
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. Norman E. Sharpless, Director, National Cancer Institute
Dr. Jeffrey S. Abrams, Acting Director for Clinical Research, Division of Cancer Treatment and Diagnosis
Dr. L. Michelle Bennett, Director, Center for Research Strategy
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. William Dahut, Scientific Director for Clinical Research, Center for Cancer Research
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Deputy Director, Division of Cancer Biology
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Sean Hanlon, Acting Director, Center for Strategic Scientific Initiatives
Dr. Ed Harlow, Special Advisor to the Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Tony Kerlavage, Acting Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies, Acting Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Mr. Jeff Shilling, Acting Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Bioinformatics and Information Technology
Ms. Donna Siegle, Acting Executive Officer, and Acting Deputy Director for Management
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. Edward L. Trimble, Director, Center for Global Health
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology Transfer Programs
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, Prevent Cancer Foundation
Ms. Paula Bowen, Kidney Cancer Association
Dr. Carol Brown, Society of Gynecologic Oncologists
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Dr. Ruth Hoffman, American Childhood Cancer Organization
Dr. Gerald F. Joseph, Jr., American College of Obstetricians and Gynecologists
Dr. Steven L. 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. Shelly Fuld Nasso, National Cancer Institute, Council of Research Advocates
Ms. Leah Ralph, Association of Community Cancer Centers
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Christy Schmidt, American Cancer Society
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Johannes Vieweg, American Urological Association
Dr. Pamela A. Wilcox, American College of Radiology
COL. (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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TUESDAY, JUNE 26, 2018

I. CALL TO ORDER AND OPENING REMARKS—DRS. ETHAN M. BASCH AND ELIZABETH M. JAFFEE

Dr. Elizabeth Jaffee called to order the 11th Joint Board of Scientific Advisors (BSA) and National Cancer Advisory Board (NCAB) meeting and welcomed members of the Board, *ex officio* members, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Drs. Ethan M. Basch and Jaffee reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the February 13, 2018 NCAB meeting was approved unanimously.

Motion. A motion to approve the minutes of the March 20, 2018 BSA meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DRS. ETHAN M. BASCH AND ELIZABETH M. JAFFEE

Dr. Jaffee called Board members' attention to future meeting dates listed on the agenda and in the Board book.

III. NCI DIRECTOR'S REPORT—DR. NORMAN E. SHARPLESS

Dr. Norman E. Sharpless, Director, NCI, welcomed BSA and NCAB members and attendees to the 11th joint meeting of these boards. He provided an update on the budget, Annual Report to the Nation, and leadership changes. Dr. Sharpless welcomed NCAB member, Dr. Nancy J. Raab-Traub back from having to be away from the Board.

Budget. Dr. Sharpless reported that Congress is working on the fiscal year (FY) 2019 budget. The House Appropriations Subcommittees on Labor, Health and Human Services, Education, and Related Agencies (LHHS) are considering the President's FY 2019 budget proposal and have conducted hearings; Dr. Sharpless testified at the House LHHS appropriations budget hearing on April 11, 2018, and the Senate LHHS briefing on May 17, 2018. He remarked that the NCI regular appropriations have increased for four consecutive years, which reflects the continued bipartisan congressional support for the NIH and NCI that remains strong. Overall, Congress appreciates the work of the NCI and is pleased to hear of the progress in cancer research. The House Appropriations LHHS Subcommittee marked up its bill to increase funding to the NCI by \$75 million (M) and to increase Cancer MoonshotSM funding by \$100 M, which raises that total to \$400 M. The Senate Appropriations Subcommittee is still revising its bill.

Dr. Sharpless reminded BSA and NCAB members that the FY 2018 enacted budget increased NCI regular appropriations by \$275 M above the FY 2017 budget. The regular appropriations do not include Cancer MoonshotSM funding. Of the \$275 M appropriated, \$40 M was allotted to technical and professional services, salaries, and benefits; \$10 M was a Small Business Innovation Research (SBIR) set-aside; \$147 M was allotted to the Research Program Grant (RPG) Pool to fully fund noncompeting type 5 awards and increase funding for Early-Stage Investigators (ESI) R01s; and \$60 M was dedicated to targeted research. Targeted research opportunities consist of a list of 20 initiatives that reflect priorities and expansion of existing efforts of the NCI Divisions and Centers. Projects include genomic profiling of

lung cancer in never-smokers in general and special populations; The Cancer Imaging Archive; data integration and analysis for the Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network; a glioblastoma research pilot project; New Onset Databases (NOD) Cohort Biorepository; and Cancer Research Education Grants to Promote Diversity (R25s).

Annual Report to the Nation. Dr. Sharpless called attention to the Annual Report to the Nation on the Status of Cancer, which was released on May 22, 2018. The overall incidence of cancer mortality decreased for men, women, and children in every ethnic and racial group. From 1999 to 2015, the death rates from cancer declined. With the advent of new immunotherapies, the NCI anticipates that this trend will continue. Although outcomes have improved for lung cancer in general and lymphoma in women, progress lags in other areas, such as obesity-associated mortality, which continues to increase. The 2018 Annual Report focuses on prostate cancer and the effect of reduced prostate-specific antigen (PSA) screening on the incidence and mortality rates, including late-stage disease. Dr. Sharpless noted that the NCI is actively monitoring the new incidence and mortality trends in prostate cancer and he encouraged reading the full report; members received a copy in the Board book.

Leadership Changes. Dr. Sharpless reported that Dr. Jeffrey S. Abrams, Acting Director for Clinical Research, Division of Cancer Treatment and Diagnosis (DCTD) announced his retirement effective December 2018. Dr. Abrams, who is recognized internationally for his efforts, has been a staunch supporter and representative of the DCTD and the NCI. Debra K. Mayer, Professor, School of Nursing, Director, Cancer Survivorship, University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, UNC–Chapel Hill, has been named Interim Director of the NCI Office of Cancer Survivorship. Dr. Mayer will serve in this capacity on a part-time basis until a new Director is selected; she commutes weekly to the NCI. Dr. Edward L. Trimble, Director, Center for Global Health (CGH), a trained obstetrician-gynecologist has agreed to lead new Global Initiative for Cervical Cancer Program with the World Health Organization (WHO), which leverages his expertise and international collaborations and relationships. Dr. Sharpless expressed appreciation to Dr. Trimble for his work in global health and his leadership of the CGH the past 7 years. He also announced that Dr. Trimble was awarded the International Gynecologic Cancer Society 2018 Global Humanitarian Award, which reflects Dr. Trimble’s interest and passion for this work. Dr. Robert T. Croyle, Director, Division of Cancer Control and Population Science (DCCPS), will serve as Acting (Interim) Director, CGH. The NCI will begin a nationwide search for a new CGH Director. Dr. Sharpless also reported that Dr. Jerry Lee, who was Deputy Director, Center for Strategic Scientific Initiatives (CSSI), has taken a new position outside of the NIH and that a search is in progress to fill that vacancy.

NCI Scientific Activities. BSA and NCAB members were informed that the NCAB *ad hoc* Working Groups—Global Health, SBIR/Small Business Technology Transfer (STTR), Data Science, and Population Sciences, Epidemiology, and Disparities—have been given their charges and are fully active. The groups are meeting in person or by teleconference to address questions and plan activities. Dr. Sharpless recognizes the time and effort necessary in supporting these working groups and conveyed NCI’s appreciation for the Board members’ continued support. He noted that the advice the NCI receives from the BSA, NCAB, and extramural community is critical to the Institute’s decision making and is highly valued.

Dr. Sharpless reminded members that the NCI was allotted \$300 M for the Cancer MoonshotSM for FY 2018, which has been implemented through the framework used in prior years and includes establishing NCI implementation teams, developing and approving concepts, and issuing funding opportunity announcements (FOAs). The NCI has issued FOAs covering each of the 10 NCAB Blue Ribbon Panel recommendations. Some projects have been active for more than 18 months and are starting to show progress.

Dr. Sharpless called attention to notable NCI research. The NCI Center for Cancer Research (CCR) investigators showed that the gut microbiome can control antitumor immune function. Dr. Stephen A. Rosenberg, Chief, Surgery Branch, CCR, engaged in a study that revises the molecular classification for the most common types of lymphoma, a culmination of his 20 years of immunotherapy research. The Cancer Genome Atlas (TCGA) Consortium completed in-depth genomic analysis of 33 cancer types known as the PanCan Atlas. In a clinical trial led by Dr. Rosenberg, the study showed that immune recognition of somatic mutations led to complete durable regression in metastatic breast cancer in a patient unresponsive to other treatments. The study has expanded to include additional patients experiencing varying degrees of remission and is emerging into a robust single-institution trial. The next steps will be to move this technology into a larger framework

Dr. Sharpless highlighted NCI's activities at the American Society of Clinical Oncology (ASCO) 2018 Annual meeting. NCI presented data on four treatment arms of the Molecular Analysis for Therapy Choice (NCI-MATCH) Trial, which showed clinical efficacy. Dr. Brigitte Widemann, Chief, Pediatric Oncology Branch, presented data on the Phase 2 study evaluating mitogen-activated protein kinase (MEK) 1 inhibitor selumetinib in children with neurofibromatosis Type 1 (NF1) and inoperable plexiform neurofibromas (PN). Patients present to the clinic with large, debilitating tumors and although not a cure, selumetinib significantly reduced tumor size, slowed tumor growth, and enabled patients to resume normal activities. The results of the Trial Assigning Individualized Options for Treatment (Rx), or TAILORx trial, were reported at the ASCO meeting. The TAILORx trial, which began enrolling patients in 2006, was a de-escalation study that correlates good outcome with less therapy, unlike most industry-sponsored trials. Results showed that more than 60 percent of women who had an intermediate risk score did not benefit from chemotherapy. Dr. Sharpless noted that TAILORx, which was partly supported by the Breast Cancer Research Stamp, led to meaningful benefit for patients, and occurred at the right time for the NCI to be involved.

NCI Key Focus Areas. Dr. Sharpless remarked on the NCI's four key focus areas—basic science, workforce development, big data, and clinical trials—where there are opportunities for progress and to accelerate cancer research. The NCI always has been interested in basic biological investigation into cancer. A renewed commitment to basic science ensures that progress and innovations are balanced across the cancer research enterprise. The NCI will continue to work to increase understanding of the biology of cancer. Increased funding to the RPG pool, which supports investigator-initiated research grants (i.e., R01s, P01s, R21s), and supporting infrastructure for the community are two broad investments in basic science. The Frederick National Laboratory for Cancer Research (FNLRCR) fosters an environment for collaboration with the NCI and has become a major component of extramural basic science. The FNLRCR-led RAS Initiative, National Cryo-Electron Microscopy (EM) Facility, and the Frederick Cell Therapy Facility are key resources. The NCI has trained a cadre of scientists, and workforce development remains at the forefront. NCI's focus is on ensuring diversity and representation, encouraging training, increasing set-aside R01 funding for Early Stage Investigators (ESIs), and implementing the Method to Extend Research Time (MERIT) award, which aligns with the broader NIH Next-Generation Researchers Initiative.

Initiatives on big data that are focused on increasing data aggregation and interpretation to speed up work across the cancer enterprise will take time to complete. The NCAB Working Group on Data Science was identified and discussed areas in which the NCI could improve and will present formal recommendations in the future. Many of the Cancer MoonshotSM initiatives focus on big data, and NCI's data infrastructure investments in cancer cloud resources, data commons, new reporting tools, and the NCI-Department of Energy (DOE) collaborations are ongoing. The NCI expanded the Surveillance, Epidemiology, and End Results (SEER) Program—its largest infrastructure investment—to include 33 percent of the American population in the cancer registries. In addition, ideas for integrating electronic health records and claims data to SEER are being discussed. Regarding clinical trials, in addition to the

traditional NCI National Clinical Trials Network (NCTN) trials, the NCI is heavily focused on conducting basket-like precision trials that include the MATCH, Pediatric MATCH, Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST), Improving Management of Symptoms Across Cancer Treatments (IMPACT), and The Molecular Atlas of Lung Development Program (LungMAP) trials. Dr. Sharpless called attention to the NCI and Veterans Affairs (VA) Interagency Group to Accelerate Trials Enrollment (NAVIGATE), which is NCI's recommitment to increase VA patient enrollment in NCTN trails.

Questions and Answers

Dr. Jaffee asked about ways that the NCI-designated Cancer Centers might incorporate a formalized educational component that integrates with other NCI programs to improve the biomedical workforce for the future. Dr. Sharpless, as a former Cancer Center director, explained that incorporating an educational component is an unfunded mandate; therefore, Cancer Center directors take different approaches to address education in their respective Centers. Currently, most Cancer Centers utilize an educational coordinator and are better organized. Through various funding mechanisms (e.g., K01s, F32s or T01s), the NCI supports investigators, graduate students, and postdoctoral fellows; and, supporting awards to the Cancer Centers aligns with NCI's mission. Dr. Sharpless emphasized that Cancer Centers are interested in workforce diversity and training and are proposing ideas to the NCI. He anticipates the Cancer Centers' being valuable partners to the NCI regarding workforce development.

Dr. Kevin M. Shannon, American Cancer Society Research Professor, Roma and Marvin Auerback Distinguished Professor in Molecular Oncology, Department of Pediatrics, School of Medicine, University of California, San Francisco, observed that a large percentage of the FY 2018 appropriation funds were allotted for targeted research and other initiatives. Dr. Shannon asked whether there had been discussions in the NCI on dedicating more funds to the RPG pool since the Cancer MoonshotSM funding already is targeting resources and is increasing paylines for established investigators. Dr. Sharpless noted that the FY 2018 additional funds added to the RPG pool—\$147 M—is a substantial increase over prior years and that most of the funds support long-term projects (e.g., 4 to 5 years). He informed members that care must be taken not to increase RPG allocations too rapidly, or the funds will be insufficient to support all awards through the project life cycle. Dr. Sharpless remarked that the NCI is committed to supporting extramural science to the highest extent possible and fully funding noncompeting awards is one such example. The NCI would like to do more and is investigating other options. Within the NIH, the NCI has lower R01 success rates than other Institutes and Centers (ICs) because of the Cancer Centers and other large programs it supports. Dr. Douglas R. Lowy, Deputy Director, NCI, added that the NCI supports more Type 1 R01 awards than the NIH, in general. The success rate for new (Type 1) awards is substantially lower NIH-wide than it is for competing (Type 2) awards. Dr. Lowy further commented that although the RPG is underfunded to an extent, overall, the additions to the RPG pool in the past 2 to 3 years have been the highest in NCI's history.

Dr. James V. Lacey, Jr., Director and Professor, Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute, City of Hope, suggested focusing workforce development efforts across all career levels, not only on mid-career or junior faculty.

Dr. Dafna Bar-Sagi, Vice Dean for Science, Senior Vice President, Chief Scientific Officer, Professor, Department of Biochemistry and Molecular Pharmacology and Medicine, New York Langone Medicine Center, New York University School of Medicine, asked about plans to collaborate with other NIH ICs to enrich the workforce pool. Dr. Sharpless noted the current inter-IC collaborations, including the NIDDK NOD study of pancreatic cancer, the biology of cancer in aging studies by the National Institute on Aging, and other Common Fund large-scale projects. Dr. Bar-Sagi suggested developing a

communications structure to inform extramural investigators of joint NCI-IC initiatives and funding opportunities.

Dr. Basch observed that private entities are arranging with Cancer Centers for exchanges of data for dashboards and asked about SEER's role in aggregating Cancer Center electronic health records data. Dr. Croyle explained that the challenge is to determine the appropriate position of the various organizations and stakeholders. The objectives are to capitalize on SEER's unique capabilities (e.g., population-based data); learn from the private sector successes; and ensure that SEER provides open, free access and publicly available data to the research community, regardless of formal partnerships with the private sector.

Dr. Cheryl L. Willman, The Maurice and Margaret Liberman, Distinguished and Endowed Chair in Cancer Research, University of New Mexico (UNM) Distinguished Professor of Pathology, UNM School of Medicine, Director and CEO, UNM Comprehensive Cancer Center, UNM, suggested establishing a SEER Working Group to assess the feasibility of developing pilot projects that leverage existing NCI-designated Cancer Center SEER efforts. Also, a focus on harmonizing SEER data and research opportunities across the United States and abroad is crucial, as is investing in mechanisms to collect data on disease recurrence in SEER.

Dr. Sylvia Katina Plevritis, Professor, Department of Radiology, Department and Biomedical Data Science, Co-Chief, Integrative Biomedical Engineering Informatics at Stanford, Stanford University School of Medicine, lauded the NCI in responding to the longer training periods and asked about efforts to determine why this is occurring. Dr. Michelle Bennett, Director, Center for Research Strategy, explained that based on the NCI's data, multiple factors are involved in the increasing age to a first R01, including the removal of the mandatory retirement age in academia or the doubling of the NIH budget.

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

Ms. M.K. Holohan, Director, Office of Government and Congressional Relations (OGCR), reported on the budget and appropriations; congressional hearings, congressional engagement, and visits; and other legislation of interest. She called attention to the detailed legislative report contained in the Board's meeting book. The FY 2018 appropriations were awarded in March 2018. During FY 2018, there have been five continuing resolutions (CRs) and two government shutdowns. Congress approved a 2-year budget agreement on February 8, 2018, that raised the debt limit; increased the budget discretionary spending cap; and includes a \$2 B increase for the NIH. Appropriators modified their proposed FY 2018 spending bills that considered the new set-asides for special topics and priorities, including opioids, infrastructure, and veterans. The NIH set-aside guarantees a \$1 B increase in both FY 2018 and FY 2019.

Ms. Holohan reminded members that the FY 2018 Omnibus signed into law March 23, 2018, increased funding for the NIH by \$3 B and to the NCI by \$275 M over the FY 2017 enacted. The NCI has received \$300 M in allocations for the Cancer MoonshotSM for FY 2018. In addition, the Omnibus included targeted increases to the NIH for opioids and pain research, Alzheimer's, Brain Research through Advancing Innovative Neurotechnologies[®] (BRAIN) Initiative, the *All of Us* Research Program, antimicrobial resistance, and the universal flu vaccine. The President's FY 2019 budget was released, along with an addendum, on February 12, 2018, increasing NIH funding from \$25.6 B to 34.8 B. Also included was a \$10 B U.S. Department of Health and Human Services (HHS)-wide request for opioids, of which, \$750 M is budgeted for the NIH; full funding for the Fogarty International Center; and consolidation of the Agency for Healthcare Research and Quality (AHRQ) and other agencies into NIH. No changes were made to the current policy related to indirect costs. The Chairman of the House Appropriations LHHS Subcommittee, Representative Thomas J. Cole of Oklahoma, and the Chairman of

the Senate Appropriations LHHS Subcommittee, Senator Roy Blunt of Missouri, noted that they were pleased to be able to provide a \$3 billion increase for the NIH in FY 2018.

Dr. Sharpless joined Dr. Francis S. Collins, Director, NIH, and other IC Directors to testify at the LHHS budget hearing on April 11, 2018. The hearing was positive. Dr. Sharpless also testified at the Senate LHHS Appropriations Subcommittee budget hearing on May 17, 2018. On June 26, 2018, the House LHHS Appropriations Subcommittee marked up its bill to increase funding for the NIH by \$1.25 B and to the NCI by \$71 M. The markup also appropriates \$400 M to the NCI for the Cancer MoonshotSM per the 21st Century Cures Act. The Senate Appropriations Subcommittee will mark up its bill after the July 4 recess. Ms. Holohan announced that the Appropriations Homeland Security Subcommittee has new leadership in both chambers: Representative Kevin Yoder of Kansas in the House and Senator Shelly Moore Capito of West Virginia in the Senate.

Ms. Holohan provided an update on congressional visits. On May 1, 2018, Rhode Island Senator Jack Reed (D) visited the NIH Clinical Center and participated in a roundtable discussion on childhood cancer research with members of the Pediatric Oncology Branch (POB), CCR, including Dr. Brigitte Widemann, Chief, POB. The Senator then met with Dr. Widemann, one of her patients who is enrolled in a chimeric antigen receptor (CAR) T-cell clinical trial, and the patient's parents. On May 30, 2018, the OGCR hosted at the NCI, for the fourth year, a bicameral, bipartisan group of 10 congressional staffers who are interested in pediatric cancer research. They toured laboratories and visited with NCI's Pediatric Oncology Branch and met a patient of Dr. Nirali Shah; they then met with National Institute of Deafness and Other Communications Disorders investigator Dr. Lisa Cunningham and learned about platinum-based therapies for hearing loss.

Ms. Holohan noted other legislation of interest to the NCI. The Childhood Cancer Survivorship, Treatment, Access and Research (STAR) Act passed the House and Senate with overwhelming support and was signed into law in June 2018. The Childhood Cancer STAR Act focuses on childhood, adolescent, and young adult biospecimen collection; addresses pediatric cancer research, and addresses including pediatric oncology expertise on the NCI Advisory Boards, which now is a requirement for the NCAB. The Research to Accelerate Cures and Equality (RACE) for Children Act, which was signed into law August 2017 can require a pediatric study plan for drugs substantially relevant to the pediatric population that are under U. S. Food and Drug Administration (FDA) review. The new provisions of the Act require the FDA, in consultation with the NCI, to develop a list of molecular targets relevant and irrelevant to pediatric cancer and to make the list public. Two public meetings were held this spring. Prior to the public meetings, the NCI issued a request for information (RFI) soliciting input from the community. A report is due in August 2018.

Ms. Holohan discussed key aspects of the 2018 midterm elections. All members of the House and one-third of the Senate will be running for reelection in November 2018. Historically, the President's party loses seats in the midterm elections. Appropriators are working to pass bills and complete their agenda prior to the elections. Midterm elections also could affect committee representations.

V. RECOGNITION OF RETIRING BSA AND NCAB MEMBERS—DR. NORMAN E. SHARPLESS

On behalf of the NCI, Dr. Sharpless 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. The following BSA members are retiring: Dr. Chi V. Dang, Scientific Director, Ludwig Institute for Cancer Research, Professor, The Wistar Institute; Dr. Ethan M. Basch, Professor of Medicine, Division of Oncology, School of Medicine, Professor of Public Health, Department of Health Policy and Management, Gillings Global School of Public Health, Director, Cancer Outcomes Research

Program, Co-Leader, Cancer Prevention and Controls Program, Lineberger Comprehensive Cancer Center, UNC at Chapel Hill; Dr. Arul M. Chinnaiyan, Director, Michigan Center for Translational Pathology, S.P. Hicks Endowed Professor of Pathology, Professor of Urology, Investigator, Howard Hughes Medical Institute, American Cancer Society Research Professor, University of Michigan Cancer Center, University of Michigan School of Medicine; Dr. Karen M. Emmons, Dean for Academic Affairs, Office of the Dean, Harvard T.H. Chan School of Public Health; Dr. Maria Elena Martinez, Professor, Department of Family Medicine and Public Health, Program Leader, Reducing Cancer Health Disparities, Sam M. Walton Endowed Chair for Cancer Research, Moores Cancer Center, University of California, San Diego; Dr. Luis F. Parada, Albert C. Foster Chair, Director, Brain Tumor Center, Member, Cancer Biology and Genetics Program, Attending Neuroscientist, Department of Neurology and Department of Neurosurgery, Memorial Sloan Kettering (MSK) Cancer Center; Ms. Mary Lou Smith, Co-Founder, Research Advocacy Network; and Dr. Cheryl L. Walker, Director, Center for Precision Environmental Health, Professor, Department of Molecular and Cellular Biology, Baylor College of Medicine.

On behalf of the NCI, Dr. Sharpless recognized the contributions made by members of the NCAB whose terms of office have expired. He expressed appreciation for their service and dedication over the course of their terms. The following NCAB members are retiring: Dr. Elizabeth M. Jaffee, Deputy Director, The Sidney Kimmel Comprehensive Cancer Center, The Dana and Albert “Cubby” Broccoli Professor of Oncology, Co-Director, Skip Viragh Center for Pancreas Cancer, Johns Hopkins University; Dr. David C. Christiani, Elkan Blout Professor of Environmental Genetics, Department of Environmental Health, Department of Epidemiology, Harvard T.H. Chan School of Public Health, Professor of Medicine, Harvard Medical School; Dr. Judy E. Garber, Director, Center for Cancer Genetics and Prevention, Dana–Farber Cancer Institute, Professor of Medicine, Harvard Medical School; 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, Professor, Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles; Dr. Mack Roach III, Professor of Radiation Oncology and Urology, Director, Particle Therapy Research Program and Outreach, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center; and Dr. Charles L. Sawyers, Chairman, Human Oncology and Pathogenesis Program, MSK Cancer Center, Investigator, Howard Hughes Medical Institute, Professor of Medicine, Weill Cornell Medical College.

VI. NEXT-GENERATION SEQUENCING (NGS) COVERAGE DETERMINATION—DRS. GIDEON BLUMENTHAL, REENA PHILIP, AND KATHERINE SZARAMA

FDA Approval of NGS-Based Oncopanel. Dr. Reena Philip, Director, Division of Molecular Genetics and Pathology, Office of *In Vitro* Diagnostic Devices and Radiological Health Center, FDA, provided an overview of the FDA regulatory process for devices and gave a regulatory update on NGS-based oncopanels. She explained that FDA’s risk-based regulation (1) considers the risks to patients if the results are wrong, (2) is dependent on the indications for use (e.g., screening or monitoring), and (3) involves risk mitigation (commonly referred to as controls). The controls in this context refer to a set of requirements or guidance put in place to help assure that a device performs safely and effectively. Three types of controls exist: general, special, and postmarket. General controls are the design controls and labeling; special controls provide evidence of a validation in submission.

The three risk-based classifications for devices are Class 1, low risk; Class 2, moderate risk; and Class 3, high risk. Class 1 devices are exempt, use general controls, and do not require a submission to the FDA. Class 2 devices can be exempt, low, or moderate risk; use general or special controls; and may or may not require a submission. Class 2 moderate risk devices require special controls, which are existing methods enumerated by the sponsor or FDA and include guidance documents consisting of performance specifications and labeling instructions. A 510(k) submission (i.e., premarket notification) is required.

Once approved and accepted by the FDA, the device/test is cleared. Class 3 devices require a complete demonstration of safety and efficacy and are subject to premarket approval (PMA), which by statute is reserved for medical devices that support or sustain human life. Dr. Philip described examples of cancer-relevant moderate Class 2 cleared tests (e.g., NGS-based tumor profiling tests) and companion diagnostics (CDx), which are Class 3 devices. CDx are *in vitro* diagnostic devices and require analytical and clinical validation.

Dr. Philip detailed the evolution of the FDA NGS regulation. As single-test, multiple biomarkers, or multiple indications, NGS-based oncopanels are increasingly being used in the clinical setting. Although a single panel can be used for multiple indications and could potentially detect rare and novel variants, demonstrating the analytical validity for each variable is challenging. To address these issues, the FDA held a public workshop on February 25, 2016. Subsequently, Foundation Medicine's FoundationFocus CDx_{BRCA} Assay for qualitative detection of *BRCA1* and *BRCA2* mutations in ovarian tissue was the first FDA-approved NGS CDx in December 2016. In June 2017, the Praxis Extended RAS Panel from Illumina, Inc., for qualitative detection of 56 specific mutations in the *RAS* gene in colorectal cancer was approved. Also in June 2017, FDA approved the first multiple biomarker test, the Thermo Fisher Oncomine™ Diagnostic (Dx) Target Test for detecting single-nucleotide variants and deletions and 23 genes in non-small cell lung cancers.

Dr. Philip emphasized that the Oncomine Dx test had CDx indications but there were no associated clinical data, which barred physician access to the test. To address this issue, the FDA established a new Class 2 regulatory pathway specific to NGS-based tumor profiling tests to reduce the burden on test developers, streamline the regulatory assessment, and modernize the approach for innovative products. Prior to establishing this new approach, the FDA partnered with the New York State Department of Health (NYSDOH) and the MSK Cancer Center to determine the least burdensome strategy. In so doing, this effort leverages the NYSDOH's Clinical Laboratory Evaluation Program and MSK's Integrated Mutation Profiling of Actionable Cancer Targets (IMPACT™) Assay, which they volunteered for NGS tumor profiling validation. At the FDA, November 15, 2017, is memorable for two reasons. First, the FDA announced the MSK IMPACT *de novo* authorization, establishing the new Class 2 Regulatory Pathway. Second, the FDA announced the recent accreditation of the NYSDOH as an FDA third-party reviewer of *in vitro* diagnostics, including tests similar to the MSK IMPACT NGS test. These tumor-profiling tests are now eligible for 510(k) clearances that can be obtained by applying directly to the FDA or to an accredited third party, such as NYSDOH; the FDA makes the final decision.

The new Class 2 regulatory pathways are a three-tiered approach to somatic NGS tests based on three levels of evidence categories that include Level 1, CDx; Level 2, cancer mutations with evidence of clinical significance; and Level 3, cancer mutations with potential clinical significance. This least burdensome pathway allows fluid reporting, future modifications, and use of quality metrics as surrogates. Dr. Philip reviewed the MSK-IMPACT tumor profiling intended-use criteria, future NGS tumor profiling assay submission requirements, and the key points of the successful FDA-NYSDOH-MSK collaboration in advancing NGS to the clinical setting, all of which were first-time efforts for the FDA.

Dr. Philip explained the two pathways for FDA approval. Premarket application to the FDA is appropriate for oncopanels with companion Dx and also can be made with Level 2 or Level 3 claims. Follow-on tests or new tests for already-approved Dx indications will be needed. The intended-use patient population as originally approved should remain unchanged. The analytical and clinical performance should be comparable, and the procured clinical sample set must be the same as the target population. The 520(k) pathway is stipulated for Level 2 and Level 3 claims only, and submissions can be directly to the FDA or to an FDA-accredited third-party reviewer, such as NYSDOH. Third party reviewers use the

same criteria as the FDA; after the third-party review, the FDA has 30 days to make a determination, whereas for a direct submission, the FDA has 90 days.

In a premarket application to the FDA, Foundation Medicine submitted its FoundationOne CDx™ (F1CDx) assay for NGS tumor profiling accreditation for five tumor indications, genomic profiling of 324 genes, and microsatellite instability (MSI) and tumor mutational burden (TMB) assessments. The assay was designated breakthrough by the FDA and received an FDA-Centers for Medicare & Medicaid Services (CMS) parallel review. On November 30, 2017, the FDA approved the Foundation One CDx™ assay, which coincided with the CMS Decision Memorandum on the national coverage for NGS for Medicare beneficiaries with advanced cancer. Dr. Philip reviewed the F1CDx indications, differences in tumor profiling and CDx assays, and FDA guidance documents for *in vitro* diagnostics and NGS.

Medicare’s NGS Coverage Determination. Dr. Katherine Szarama, Presidential Management Fellow, CMS, explained that the Coverage and Analysis Group’s (CAG’s) contains four divisions that develop and implement the CMS National Coverage Determinations (NCDs) and other policies. As controlling authority for Medicare contractors and adjudicators, the HHS Secretary has the discretionary decision to determine whether or not a particular item or service is covered nationally under the Social Security Act (or Act). In the absence of an NCD, Medicare Administrative Contractors (MACs) may establish a local coverage determination (LCD) in their respective jurisdictions.

Dr. Szarama detailed the four requirements for an NCD. The item or service must be legal; Congress must have given a Medicare benefit category for the item or service; the item or service must be reasonable and necessary; and coding and payment instructions are needed. Congress defined both specific and broad benefit categories. This meeting’s discussion focused on what the Section 1861(s)(3) of the Social Security Act broadly defines as other diagnostic tests. Dr. Szarama emphasized that assigning a benefit category is not an indication that the item or service will be covered by Medicare, but it permits Medicare to continue with the coverage determination process. Medicare defines screening as the application of a test to people who currently have no symptoms of a particular disease. Congress, under Section 861(ddd)(1) of the Act, assigned an additional benefit category for additional preventive services that are recommended as Grade A or Grade B by the U.S. Preventive Services Task Force (USPSTF).

Two authorities address coverage for items or services that are deemed reasonable and necessary. Act 1862(a)(1)(A) states that no payment may be made for items or services that are not reasonable and necessary for the diagnosis or treatment of illness or injury. For diagnostic services, adequate evidence of analytical and clinical validity is required. Act 1862(a)(1)(E) states that no payment may be made for items or services that are not reasonable and necessary in the case of research. This research authority is vested with the Administrator of the AHRQ with respect to the outcomes, effectiveness, and appropriateness of health care services and procedures.

Dr. Szarama provided an overview of the Medicare national coverage process. An NCD is completed during a 6- to 9-month period and consists of the request, staff review, posting of the proposed decision memorandum, 30-day public comment period, and the final decision memorandum. This process can be accelerated using a parallel path, or increased by involving the Federal Advisory Committee Act (FACA) Medicare Evidence Development and Coverage Advisory Committee (MEDCAC), which was established to provide independent guidance, expert advice, and through technology assessment. Dr. Szarama reiterated that CMS posted its proposed NGS decision memorandum on November 15, 2017, which coincided with the FDA approval of the NGS F1CDx assay. The 30-day public comment period was open from November 30, 2017, to January 17, 2018, and the final decision memorandum was

delivered to the HHS Secretary on March 16, 2018. The final decision includes specifications on the coverage, intended patient, diagnostic test, and contractors.

Dr. Szarama explained that coding and payments are made according to fee schedules and payment systems, and more than 16 exist in the Medicare program. Common health care procedural codes are necessary, and laboratory tests are generally paid using the physician fee schedule (PFS) or the clinical laboratory fee schedule (CLFS). Pricing was previously determined as the lower of the contractor pricing (e.g., cross walking or gap filling) or nationally established rate. CMS updated its payment rates as a result of the Protecting Access to Medicare (PAMA) Act of 2014. Section 216(a) of PAMA specifically pertains to clinical diagnostic laboratory tests. Further details on the NGS NCD and CMS payment systems are available on the CMS website.

Questions and Answers

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Department of Medicine, Washington University School of Medicine in St. Louis, recognizes that future submissions for NGS test approvals will likely be tests designed by individual innovators and will focus primarily on persistent disease rather than specific mutations. He inquired about ways to protect the innovative space of investigators and academic institutions. Dr. Ley also commented that Institutional Review Boards are challenged in dealing with these issues and are seeking FDA's advice. Dr. Philip explained that a laboratory-developed test is under the authoritative discretion of the owner(s). An institution or investigator elects to bring a test to the FDA, but is not required to do so unless it has been deemed necessary. Much of the confusion centers on whether the device is for investigational use and whether the associated risks are significant; the FDA guidance document contains a section that clarifies risk. Roughly 10 percent of the devices reviewed by the FDA have significant risk; the majority have insignificant risk. It is the FDA's intent that the Investigational New Drug application would be sufficient to resolve these issues. Also, the FDA Oncology Center of Excellence (OCE) was formed to be the interface in making such decisions.

Dr. Michael John Becich, Chairman and Distinguished University Professor, Department of Biomedical Informatics, Professor, Pathology, Information Sciences, Telecommunications and Clinical/Translational Sciences, Associate Vice Chancellor for Informatics in the Health Sciences, Director, Center for Commercial Application of Healthcare Data, Associate Director for Cancer Institute, Associate Director, Clinical and Translational Science Institute, University of Pittsburgh School of Medicine, asked about regulatory guidance or documentation for specifications on compassionate use of genomic expression data or biomarker data-related software being used for algorithm-based matching to drugs and treatment. Dr. Philip noted that FDA is actively evaluating software as medical devices; guidance does exist, which she can forward to the NCI. For the sake of time, that information was not included in today's presentation. The key determinant is that if the software provides information that a physician can easily transfer, then an FDA submission is not necessary.

Dr. Eileen P. White, Chief Scientific Officer, Deputy Director, Associate Director for Basic Research, Rutgers Cancer Institute of New Jersey, Distinguished Professor, Molecular Biology and Biochemistry, Rutgers, The State University of New Jersey, sought clarity on which clinical databases were eligible for developers' use in validating Class 3 devices. Dr. Philip pointed out that discussions are ongoing in the OCE on this topic and that the FDA is working on ways to use real-world evidence data from approved tests when clinical data are not available. An FDA internal working group makes decisions on databases, and overseers or owners of a database are asked to complete the pre-submission process.

In response to a query from Dr. Willman on the observation that approvals for recurrent or late-stage malignancy, which significantly impact patient survival, are not being considered in CMS

deliberations, Dr. Szarama pointed out that the decision based on the evidence made available to the CMS was on those indications in patients with advanced cancers. The opportunity exists to expand coverage through the proposed decision on coverage with evidence development, and the CAG is actively seeking input from those interested in developing evidence on items and services for early-stage cancers.

Dr. Garber asked whether regulations prohibit reanalyzing patient tumors following various rounds of treatments. Dr. Szarama explained that the limitations in the final coverage determination were based on the evidence. CMS had not received studies of patients receiving the same diagnostic laboratory test more than once, which is reflected in the final decision. This can be changed through a reconsideration of the existing NCD or through a different NCD/diagnostic test. Dr. Ley commented that tumor biology supports repeat testing and that a critical part of using NGS tumor profiling tests is having the ability to assess response to treatment. Dr. Szarama noted that the different diagnostic laboratory tests are limited to the NCD, as are the coding and payment. The CAG has noticed that each diagnostic laboratory test has developed a proprietary laboratory analysis code in partnership with the American Medical Association. Dr. Becich commented that given what is known about tumor evolution, being limited to one-time testing seems scientifically unwise.

VII. T-CELLS AS A DRUG FOR THE PERSONALIZED IMMUNOTHERAPY OF CANCER—DR. STEVEN A. ROSENBERG

Dr. Steven A. Rosenberg discussed his recent research and establishing a blueprint for the application of immunotherapy to epithelial cancers. He noted that the major challenge confronting cancer immunotherapy is the development of effective immunotherapies for patients with metastatic epithelial solid cancers that result in 80 percent of cancer deaths seen today. There are many advantages to using cell transfer therapy compared to using individual drugs, which include administering large numbers of highly selected cells that recognize tumor cells, administering cells activated *ex vivo* that exhibit anti-tumor effector function, identifying the specific cell function in a lymphocyte that is required for cancer, and manipulating the host prior to cell transfer to provide an altered microenvironment for transferred cells.

Dr. Rosenberg detailed adoptive cell therapy (ACT) methods his laboratory developed for melanoma, which have provided insight into the development of treatment for the common forms of cancer. The ACT process using tumor-infiltrating lymphocytes (TIL) begins by excising a tumor and culturing *in vivo*; identifying cultures with potential anti-tumor activity and/or cultures that are growing well; and administering active cultures to patients after lympho-depleting chemotherapy. To date, 194 patients with metastatic melanoma have been treated with ACT over the past 10 years. The objective response (OR) rate was 55 percent and the complete response (CR) rate was 24 percent. Dr. Rosenberg highlighted two key observations. First, in achieving a CR in 46 of the 194 melanoma patients using ACT, only 2 percent had a recurrence. The CR is maintained in the 44 patients more than 10 years after treatment. Second, of the 46 CRs, only 2 percent received more than a single treatment (i.e., one cell infusion). ACT cells can potentially expand up to 1,000-fold 7 to 10 days after infusion and cells exhibiting anti-tumor activity can achieve effector function. In fact, the overall survival of patients with metastatic melanoma that were treated with autologous TIL and interleukin 2 (IL-2) was 35 percent; however, ACT appears to eliminate the last of (or deactivate) the melanoma cell. The next steps were to determine the mechanisms associated with TIL recognition in melanoma cell destruction.

The specific cancer regression in the absence of off-tumor/on-target toxicities (i.e., no normal tissue damage) in metastatic melanoma patients led the Rosenberg laboratory to explore the role of specific cancer mutations as TIL targets. They developed approaches to mine the cancer exome to identify immunologic cancer mutations. In general, for a mutation to be a cancer antigen, it has to be processed intracellularly into a nine to 11 amino peptide, which must be presented on one of the patient's surface

major histocompatibility complex (MHC) molecules; only rare mutations will be antigenic. The Rosenberg laboratory developed a blueprint for the generation of mutation reactive T-cells in common cancers and began with melanoma. The blueprint involves isolating genomic DNA and RNA from excised patient tumors; performing whole exome and transcriptome sequencing to identify mutations; and synthesizing mutated tandem minigenes (TMGs) that encode 25 mers containing all mutations. The TMGs are introduced into the patient's antigen presenting cells (APCs)—a dendritic cell—and the APCs express all class 1 and 2 MHCs of that patient. The TILs that have manifested from the complete regression of all the patient's metastatic cancer are incubated with APCs to determine whether there is TIL mutation recognition. The advantages of this approach are that peptide binding to the MHC is not needed, candidate peptides and all MHC loci are incident on the screen, and tumor cell lines are not necessary.

Using the TMG approach, the Rosenberg laboratory first investigated the immunogenic mutations in a melanoma patient who had 71 non-synonymous mutations in a single amino acid change. They found that the kinesin family member 2C (KIF2C) mediated the complete regression of the patient's cancer. Further assessments in 22 consecutive melanoma patients revealed 54 immunogenic neoepitopes; 82 percent of patients had mutation reactive T-cells in TIL; 1.4 percent of mutations screened were immunogenic; and 63 percent of patients with melanoma recognized two or more immunogenic mutations. The preliminary conclusions were that ACT mediates complete durable, and likely curable, regression of metastatic melanoma based on the immunogenic cancer mutations.

The Rosenberg laboratory next determined whether antigens in common epithelial cancers could be targeted by cell-based immunotherapy. He reported on patients with epithelial cancers (e.g., colorectal and breast cancers) treated using the TMG approach who had been unresponsive to prior treatments. Ninety-nine patients were screened, 81 percent of patients had mutated antigens recognizable by TILs, and all neoantigens were unique except for two KRAS antigens. These findings led to the hypothesis that recognition of random somatic mutations is the final common pathway explaining cancer regression from most immunotherapies for solid cancers. Dr. Rosenberg further demonstrated the utility of the TMG approach in metastatic breast and cervical cancers; described data depicting the blueprint for cancer immunotherapy directed against the common epithelial cells; and potential improvements in targeting somatic mutations of epithelial cancers. He concluded that cell transfer therapy can mediate durable regressions in patients with metastatic cancer refractory to other treatments. T-cells that recognize unique somatic mutations can be found in TIL and peripheral blood of patients with common epithelial cancers. Identification and targeting mutations unique to each cancer or shared mutation (e.g., KRAS or p53) has the potential to extend cell therapy to patients with common epithelial cancers.

Questions and Answers

Dr. Max S. Wicha, Deputy Director of the Taubman Institute, Distinguished Professor of Oncology, Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan, asked about evidence of a bystander effect contributing to the response of targeting non-driver mutations. Dr. Rosenberg explained that the approach to overcome downregulation of some antigens or appearance of new some mutations is to target multiple mutations simultaneously, but he was not aware of evidence supporting a bystander effect.

In response to a query by Dr. Shannon on the low number of patients having the common cooperating mutations (e.g., KRAS K12D) in colorectal cancers, Dr. Rosenberg pointed out that the mutation must fit and be presented in the patient's MHC molecule to be recognized, which could be a possible explanation. Data on the 99 patients with epithelial cancers are still under review.

Dr. Mayer asked how well patients tolerated the treatment and whether there had been any unforeseen late effects. Dr. Rosenberg responded that the TMGs are targeting specific mutations and the effect of normal cells is minimal. Side effects related to the lymph node depleting chemotherapy have been observed and the average patient hospital stay is 8 to 10 days. Also, toxicity from IL-2 has been reported and doses are therefore limited to five or less.

In response to a query by Dr. Jaffee on the duration of T-cells following treatment and induction of endogenous T-cells, Dr. Rosenberg replied affirmatively that reactivity against untargeted antigens can be detected in the peripheral blood of patients that previously were undetected.

Dr. Christopher M. Counter, Professor, Department of Pharmacology and Cancer Biology, Duke University School of Medicine, asked whether post-translational modifications (PTMs) had been observed in the peptides. Dr. Rosenberg explained nonsynonymous mutations are the only modifications they have observed; plus, PTMs will not be picked up as mutations in the TMG approach.

VIII. ONGOING AND NEW BUSINESS—DRS. ETHAN M. BASCH AND ELIZABETH M. JAFFEE

NCAB *Ad Hoc* Subcommittee on Population Sciences, Epidemiology, and Disparities.

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, provided a report of the June 25, 2018 *Ad Hoc* Subcommittee on Population Sciences, Epidemiology, and Disparities. The Subcommittee heard updates on two of the four key focus areas they previously identified: cancer research training programs and the NCI portfolio on survivorship research. Dr. Jonathan Wiest, Director for the Center for Cancer Training (CCT), provided an overview of CCT's training programs, including a detailed report on the changes in funding mechanisms for mentored awards. There were discussions on data on success rates of applications by scientific discipline, which revealed that the population science community is submitting less grants to the transition mechanisms. The Subcommittee suggested ways to increase awareness and will work with the NCI on this effort. There also were discussions on the elimination of R25Ts, transitioning to T32s, focusing on investigator funded awards, and establishing a new funding mechanism for early career researchers. The Subcommittee also heard a presentation by Dr. Paul Jacobsen, Associate Director, Healthcare Delivery Research Program, DCCPS, on cancer survivor and survivorship research at the NCI. From prior Subcommittee recommendations, an *Ad Hoc* Working Group on Strategic Approaches and Opportunities in Population Science, Epidemiology, and Disparities was established. The Working Group met for its first in-person meeting and was given the charge by Dr. Sharpless. Future teleconference meetings are in progress and a face-to-face meeting is being planned for the fall of 2018.

Questions and Answers

Dr. Plevritis pointed out that data on recurrence is not collected in SEER and therefore is challenging to study.

In response to a query from Dr. Basch on the impact to population scientists in the ending of the K07 program, Dr. Wiest explained that the K07 supported late-stage investigators and was not helping with career development to any large degree. It also extended time to a first R01, which is not NCI's goal. Dr. Wiest clarified that the number of funding mechanisms changed and not the number of awards being issued.

Motion. A motion to accept the report of the June 25, 2018 NCAB *Ad Hoc* Population Science, Epidemiology, and Disparities Subcommittee meeting was approved unanimously.

NCAB *Ad Hoc* Subcommittee on Global Cancer Research. Dr. Francis Ali-Osman—Margaret Harris, and David Silverman, Distinguished Professor of Neuro-Oncology Research, Professor of Surgery, Professor of Pathology, Department of Surgery and Pathology, Duke University Medical Center and Chair of the NCAB *Ad Hoc* Global Cancer Research Subcommittee—presented the report of the June 25, 2018 Subcommittee meeting. NCI Director Dr. Norman Sharpless summarized the global HPV/cervical cancer initiative with the WHO and pending changes in the Center for Global Health (CGH) personnel. The Subcommittee then heard a more detailed update from Dr. Trimble, Director, CGH, on the new NCI HPV/cervical initiative. 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 and co-chair of the *Ad Hoc* Working Group on Global Health (GH)—presented a status report on the activities of the Working Group. There also were discussions on the GH Working Group draft recommendations, which will be formalized and presented in the Working Group’s report to the NCAB at a future date. The Subcommittee expressed its appreciation to the CGH staff and leadership for the ongoing commitment to global cancer research.

Motion. A motion to accept the report of the June 25, 2018, NCAB *Ad Hoc* Global Cancer Research Subcommittee meeting was approved unanimously.

**IX. RFA/COOP. AGR. CONCEPTS—NEW AND RE-ISSUE—NCI STAFF
Office of the Director**

**Pathway to Independence Awards for Outstanding Early-Stage Postdoctoral Fellows (K88/R00)
(New RFA)—Dr. Michele McGuirl**

Dr. Michele McGuirl, Program Director, CCT, presented a new concept to establish the pathway to independence awards for outstanding early-stage postdoctoral fellows. Dr. McGuirl noted that Career development (K) awards are effective for transitioning to research independence. In fact, from FYs 2008 to 2012, 89 percent of NCI K99 awardees received tenured faculty positions and applied for R01s; of the 89 percent, 52 percent received an R01. Conversely, within the F32 mechanism, which is specifically for early-stage postdoctoral fellows, only 7 percent of awardees received an R01. Although the K99 is successful, is a proven and direct pathway to independence, and has overshadowed the F32, it does not meet the needs of the early-stage postdoctoral fellows. Further, a 2018 report from the National Academy of Sciences assessing the F and K portfolios across the NIH, came to the same conclusion as the NCI. An in-depth look at the NCI K99s revealed that 95 percent of awardees were applying in the third to fourth year of a postdoctoral fellowship.

The DCCPS analyzed R01s issued from two FOA cycles in 2017 that focused on data, population, and behavioral scientists receiving a terminal degree in 2005 and found that 50 percent in this group had received tenured track positions 0–2 years into postdoctoral research, but are not competitive for current K awards, which targets persons with 4 to 8 years of postdoctoral research experience. Also, persons receiving tenured positions early have no protected time for teaching, no assurance of a competitive startup package, and take longer to get a first R01. The NCI proposes a new transition award for early-stage postdoctoral fellows, the K88/R00 Award.

The RFAs will support two specific disciplines—population and behavioral sciences, and data science—to support the transition to independence of those assuming tenure track positions early. Outstanding postdoctoral fellows with 2 years or less research experience are eligible and an institutional nomination letter will be required. The applicant will be strongly encouraged to conduct the R00 phase of the award at an institution different from that of the K99 phase.

Subcommittee Review. Dr. Willman expressed the Subcommittee's strong enthusiasm in support of the concept and remarked on the well-written concept proposal. Dr. Willman conveyed the Subcommittee's concern that an RFA focused on specific disciplines sends the wrong message to the extramural community. Data, population, and behavioral scientists are in high demand and are receiving tenured positions early and will be biased to applying. The Subcommittee recommends that in the pilot phase, the awards not be limited to specific scientific disciplines and appreciates NCI staff responses to their questions about the review criteria.

The first year cost for the one-time issuance is estimated at \$4.8 M for 16 K88/R00 awards, with a total cost of \$24 M for 5 years.

Questions and Answers

Dr. Eileen White noted that similar initiatives such as the successful Whitehead Institute Fellows Program and the Cold Spring Harbor Laboratory Fellows Program, which support all fields of cancer research argue against a discipline-specific program. Dr. Parada added that all trainees doing relevant cancer research should have the same opportunities and that awards should not be biased to a specific discipline.

Dr. Becich suggested issuing, in the long-term, a discipline-specific RFA or similar mechanism to support data, population, and behavioral sciences.

Motion. A motion to concur on the Office of the Director's (OD's) RFA entitled "Pathway to Independence Awards for Outstanding Early-Stage Postdoctoral Fellows (K88/00)" was approved with 12 ayes, 7 nays, and 0 abstentions, with the stipulation that applications will not be discipline specific.

NCI Awardee Skills Development Consortium (NASDC) (New RFA/Coop. Agr.)— Dr. Jonathan Wiest

Dr. Wiest presented a new concept to establish an NCI awardee skills development consortium (NASDC) to address the needs of new and early-stage investigators. The NCI's competing and non-competing awards support approximately 1,600 new and early phase investigators each year. These grantees, who are at a critical stage in their career, require skills beyond those taught in schools and existing postdoctoral training, such as securing funding and managing personnel and budgets. Given that existing courses on these topics are not specifically designed for NCI grantees and that the current hypercompetitive funding climate further exacerbates the challenges of establishing a successful academic career, the CCT is proposing a NASDC. The purpose of the concept is to support the development and delivery of a suite of short courses teaching critical skills necessary for maintaining a successful independent cancer research career and to ensure that all investigators in the NCI RPG pipeline have access to opportunities and resources to assist in developing the needed skills. Also, the NASDC is expected to assist in retaining cancer research principal investigators and maximize the NCI's return on investment.

The RFA, which aligns with the NIH Next Generation Research Initiative (NGRI), will support NCI-funded K awardees and ESIs and new investigators with R00, R21, and first R01 awardees. Participants must represent a diverse workforce regarding race, ethnicity, and gender. Established NCI investigators and intramural researchers also may participate if training course openings are available.

Subcommittee Review. Dr. Martinez expressed the Subcommittee's support for the concept, which is addressing a critical gap. She noted that the Subcommittee suggested leveraging existing NCI-sponsored courses and educational workshops, such as the American Association for Cancer Research's

(AACR) Molecular Biology in Clinical Oncology Workshop and the Cancer Research Education Grants Program (R25).

The first year cost for the one-time issuance is estimated at \$1.25 M for five U25 awards and \$1.25 M for one U24 award, with a total cost of \$7.5 M for 3 years.

Questions and Answers

Dr. Becich suggested designing a course in computer programming for biologists and Dr. Lacey suggested incorporating strategies to address demand, accessibility, and sustainability.

Dr. Scott W. Hiebert, Hortense B. Ingram Chair in Cancer Research, Professor of Biochemistry, Department of Biochemistry, Vanderbilt University School of Medicine, suggested including mid-stage career investigators and encouraged including in the RFA requirements for participants to bring their data for analysis regarding a data science/statistical course.

Dr. Emmons expressed concern that a 3-year, short-term evaluation period would not be adequate to assess the NASDC.

Motion. A motion to concur on the OD's RFA/Cooperative Agreement (Coop. Agr.) entitled "NCI Awardee Skills Development Consortium (NASDC)" was approved unanimously.

U.S.-China Program for Biomedical Collaborative Research (Re-Issue RFA)—Dr. Paul Pearlman

Dr. Paul Pearlman, Health Science Policy Analyst, CGH, presented the re-issue concept of the trans-NIH U.S.-China Joint Program for biomedical collaborative research. The Program, which has been operational from FYs 2011 to 2017, was initially supported with Administrative Supplements from the National Natural Science Foundation of China (NSFC) and expanded to issuing 3- and 5-year R01s. The CGH identifies potential partners to begin the process, the trans-NIH team drafts FOAs, and CGH negotiates funding plans with the foreign partners. Dr. Pearlman emphasized that the CGH evaluated the first three rounds of the program. Thirty-seven percent of Administrative Supplement awardees and 51 percent of R01 recipients responded. The awards focused on building research capacity, fostering collaborations and accessibility to unique populations, and establishing a foundation for future collaborative research studies. Seventy-five distinct publications across 33 journals were identified; of the 75, four were published in high-impact journals.

On April 10, 2018, the NIH-NSFC Working Group met to discuss the proposed topics and budget for FY 2019. Several ICs are planning to participate in the Program, including the: National Institute of Environmental Health Sciences (NIEHS), National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Mental Health (NIMH), and National Eye Institute (NEI). The Working Group recommended three cancer topics for 2018, including cancer sites with regional high prevalence, environmental risk factors for cancer, and Traditional Chinese Medicine (TCM) and Natural Products.

This RFA reissuance will support investigations on the incidence and prevalence of nasopharyngeal, upper gastrointestinal, and liver cancers; the roles of pollution and chemical exposures in cancer; and, alternative treatments, including TCM.

Subcommittee Review. Dr. Martine F. Roussel, St. Jude Children's Research Endowed Chair in Molecular Oncogenesis, Full Professor, Department of Molecular Sciences, St. Jude Children's Research Hospital, expressed the Subcommittee's support of the concept re-issuance. The Subcommittee suggested expanding the scope and focus to include genomics and proteomics collaborations and sponsoring a

symposium that highlights China's cancer research and other research opportunities, which also would increase awareness of the NCI's efforts.

The first year cost for the one-time issuance is estimated at \$1 M for 5 awards, with a total cost of \$5 M for 5 years.

Questions and Answers

In response to queries by Dr. Jaffee on biospecimen regulations in China and intellectual property rights (IP) for the Program, Dr. Pearlman replied that a process to transfer biospecimens from China does exist, but is not easy. The key is to work out the details prior to collecting the samples. The institutions are responsible for requirements on IP.

Dr. Ian M. Thompson, Jr., President, CRISTUS, Texas Urology Group, asked about the overall goal and direction for the Program. Dr. Pearlman explained that the goal is to focus on topics of interest to the NCI Divisions and Centers that would be a good fit for the Program and lead to sustainable relationships.

Motion. A motion to concur on the OD's re-issue RFA entitled "U.S.-China Program for Biomedical Collaborative Research" was approved unanimously.

Division of Cancer Treatment and Diagnosis

Early Clinical Trials of New Anticancer Agents With Phase 1 and 2 Emphasis (Re-Issue RFA/Coop. Agr.)—Subcommittee

Subcommittee Review. Dr. Shannon expressed the Subcommittee's support for reissuance of the concept. He explained that the Early Therapeutic Clinical Trials Network (ETCTN) interacts with the NCI Experimental Therapeutics (NExT) Program to advance new agents into clinical trials. The Subcommittee confirmed with the NCI that details on monitoring site performance will be included in the RFA and also suggested including language in the RFA that encourages the participating institutions (i.e., clinical sites) to set aside funds to support training early-stage clinical investigators. Dr. Shannon commented on the ETCTN's notable trial accruals and publication record during the current funding cycle from FYs 2014 to 2018. The Subcommittee appreciates NCI staff responses to their questions.

The first year cost for the one-time issuance is estimated at \$23.7 M for 10 awards, with a total cost of \$118.5 M for 5 years.

Motion. A motion to concur on the Division of Cancer Treatment and Diagnosis' (DCTD's) re-issue RFA/Coop. Agr. entitled "Early Clinical Trials of New Anticancer Agents with Phase 1 and 2 Emphasis" was approved unanimously.

X. NCAB CLOSED SESSION—DR. ELIZABETH JAFFEE

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

There was a review of grants and a discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussions for which there was potential conflict of interest, real or apparent.

WEDNESDAY, JUNE 27, 2018

XI. CALL TO ORDER AND OPENING REMARKS—DRS. ETHAN M. BASCH AND ELIZABETH M. JAFFEE

Dr. Elizabeth M. Jaffee called to order the second day of the 11th Joint Board of Scientific Advisors (BSA) and National Cancer Advisory Board (NCAB) meeting and welcomed members of the Board, *ex officio* members, liaison representatives, staff, and guests. Dr. Jaffee stated that the agenda included a review of six BSA Cancer MoonshotSM concepts.

XII. RFA/COOP. AGR. CANCER MOONSHOT CONCEPTS—NEW—NCI STAFF

Division of Cancer Biology

**Immuno-Oncology Translational Network (IOTN) (New RFA/Coop. Agr.)—
Dr. Nancy Boudreau**

Dr. Nancy Boudreau, Chief, Tumor Metastasis Branch, Division of Cancer Biology (DCB), presented two concepts to expand the Immuno-Oncology Translational Network (IOTN). Dr. Boudreau noted that the current RFA and consortium structure include the Cancer Immunotherapy (RFA-CA-17-045) and Cancer Immunoprevention (RFA-CA-17-046) Research Projects; Data Management and Resource Sharing Center (RFA-CA-047); and the Cellular Immunotherapy Data Resource (RFA-CA-17-048). The IOTN also leverages other NCI initiatives, including the Consortium for Pancreatic Ductal Adenocarcinoma (PDAC). The NCI proposed two new FY 2019 initiatives are: Cancer Immunoprevention Research Projects and Immuno-Engineering to Improve Immunotherapy (i3) Centers.

The goal of the Cancer Immunoprevention Research Projects (U01) is to identify actionable targets arising in pre-cancerous lesions and to develop and validate early intervention vaccines based on those targets. Whereas, the prevention projects will focus on cancers that occur at specific organ sites in high-risk cohorts such as Lynch Syndrome. She stated that in the first funding cycle, 11 U01 applications were received and represented a limited number of high-risk cohorts. Several investigators cited a lack of preliminary data to support submitting a U01 application. The NCI is proposing use of the UH2/UH3 phased mechanism, which allows investigators to submit compelling research applications with minimal preliminary data. This RFA will support implementing a UH2/UH3 funding structure to enable investigators to pursue immune target discovery without the requirement for substantial preliminary data and follow-on studies from successful UH2s.

The goal of establishing i3 Centers is to support multidisciplinary teams that incorporate bioengineering and systems biology approaches in the IOTN. This RFA will support the establishment of i3 Centers to assist the IOTN with projects and administrative functions.

Subcommittee Review. Dr. Shannon expressed the Subcommittee's support for the new concepts, which will enhance the IOTN. The Subcommittee expressed appreciation to the NCI for their strategy to consider the UH2/UH3 mechanism in responding to the small number of immunoprevention U01 applications.

Questions and Answers

Dr. Jaffee suggested including a predictive neo-antigen modeling component, which would prompt multidisciplinary scientists, including structural and computational biologists and immunologists, to apply.

The first year cost for the one-time issuance is estimated at \$9.69 M for two to three UH2/UH3 awards and two to four U54 awards, with a total cost of \$48.45 M for 5 years.

Motion. A motion to concur on the DCB’s RFA/Coop. Agr. entitled “Immuno-Oncology Translation Network (IOTN)” was approved unanimously.

Division of Cancer Control and Population Sciences

Implementation Science Centers for Cancer Control (IS-C³) (New RFA)—Dr. David A. Chambers

Dr. David A. Chambers, Deputy Director, Implementation Science, Division of Cancer Control and Population Sciences (DCCPS), presented a new concept for establishing implementation science centers for cancer control (IS-C³), which leverages other NCI implementation science efforts such as the Accelerating Colorectal Cancer Screening and follow-up through Implementation Science (ACCSIS) and Improving Management of Symptoms Across Cancer Treatments (IMPACT). Dr. Chambers informed members that NCAB Blue Ribbon Panel Working Group on Implementation Science observed that many evidence based-programs regarding prevention and screening exist but are not being utilized to their full extent, especially among underserved populations. Implementation science is needed to drive the population benefit. Current approaches for scaling up implementation science are forming an implementation laboratory, developing and executing natural experiments and rapid cycle testing, generation of pilot studies, and advocating for nationwide support for implementation scientists in cancer control.

This RFA will support establishing IS-C³ centers to scale up implementation science efforts across the Cancer MoonshotSM initiatives. The Centers will consist of an administrative core, implementations science laboratories, measurement and methods core, a set of innovative research pilot projects, and a network core.

Subcommittee Review. Dr. Emmons expressed the Subcommittee’s support for the concept. She noted that the Subcommittee expressed concern regarding the size of the Centers being planned and the overall total costs. Thus, the Subcommittee suggested that the NCI review the budget and scope of the RFA.

Questions and Answers

Dr. Martinez suggested exploring potential opportunities to establish implementation science-related cancer control policy changes.

Dr. Willman suggested leveraging existing NIH data sharing efforts and networks of rural-based primary care centers experienced in implementation science.

The first year cost for the one-time issuance is estimated at \$8 M for three P50 awards and three P20 awards, with a total cost of \$40 M for 5 years.

Motion. A motion to concur on the DCCPS’ RFA entitled “Implementation Science Center for Cancer Control (IS-C³)” was approved unanimously.

Communications and Decision Making in the Context of Risk and Uncertainty for Individuals with Inherited Cancer (New RFA)—Dr. Wendy Nelson

Dr. Wendy Nelson, Program Director, DCCPS, presented a new concept on communication decision-making for individuals with inherited cancer syndromes. Dr. Nelson informed members that the goal of the RFA is to develop, test, and evaluate interventions and implementation approaches or adapt existing approaches to improve patient/provider/family risk communication and decision-making for individuals and families with an inherited susceptibility to cancer. She noted that communication is critical in the delivery of care for individuals who have inherited susceptibilities to cancer and is essential to understanding risk and managing uncertainty. Factors such as cognitive biases or cultural beliefs influence understanding risk. There are no gold standard practices for communicating risks or genetic results and communication strategies are needed to promote concordant genetic testing and follow-up health care.

The RFA will support U01 applications that develop, test, evaluate, and implement existing interventions that address patient-level communication approaches to genetic counseling, communication approaches for cancer risk disclosure, tailored strategies, and decision-making tools.

Subcommittee Review. Dr. Quale expressed the Subcommittee’s support for the concept, which addresses an important need in the cancer community.

Questions and Answers

In response to a query by Dr. Karlan on addressing the direct-to-consumer genetic counseling, Dr. Nelson responded that since it is not well known how these types of counseling are being used or interpreted, the RFA includes a research question on direct-to-consumer genetic counseling.

The first year cost for the one-time issuance is estimated at \$5 M for five U01 awards, with a total cost of \$25 M for 5 years.

Motion. A motion to concur on the DCCPS’ RFA entitled “Communications and Decision Making in the Context of Risk and Uncertainty for Individuals with Inherited Cancer Syndromes” was approved unanimously.

Research to Develop Evidence-Based Approaches to Patient Engagement (New RFA/Coop. Agr.)—Dr. Deborah M. Winn

Dr. Deborah M. Winn, Deputy Director, DCCPS, presented a new concept on research to develop evidence-based approaches to patient engagement. Dr. Winn informed members that patient engagement is considered as an ongoing bi-directional and mutually beneficial interaction between patients and researchers. The DCCPS is proposing a Direct Patient Engagement for Discovery Science Research Program consisting of three initiatives: fundamental research, demonstration projects, and a patient portal. This RFA is addressing the fundamental research initiative.

Dr. Winn stated that the purpose of the concept is to build scientific knowledge about using direct patient engagement to improve patient experiences related to participation in cancer research studies. Engaging patients as participants in research studies is influenced by complex barriers and facilitators that can be categorized as cognitive related, opportunity-based, sociodemographic characteristics, motivational, and ecological. Most of the research in this area is focused on a single category or a few of these characteristics and the work often is siloed. Gaps exist in research on patient engagement in cancer research studies. Patient engagement research could lead to improved patient participation in cancer

research studies. The objectives of this research are to fill knowledge gaps, develop and test efficacy of interventions, and explore strategies to overcome barriers.

Subcommittee Review. Dr. Basch conveyed that the Subcommittee acknowledges that engaging patients in research is essential and that the NCI has been a leader in these efforts. However, the Subcommittee expressed concern that their key recommendations had not been fully addressed and suggested that consideration should be given to refocusing the RFA scope to include clinical trial accrual and retention; clearly define the focus (e.g., health disparities or patient engagement); and, distinguish between patient engagement and patient participation.

Questions and Answers

Dr. Willman suggested leveraging other NCI studies, such as the Molecular Analysis for Therapy Choice (MATCH) trial; conveying the overall benefit to patients; and, re-calculating the budget to support the scope of work.

The first year cost for the one-time issuance is estimated at \$2.5 M for five U01 awards, with a total cost of \$12.5 M for 5 years.

Motion. A motion to defer on the DCCPS' RFA/Coop. Agr. entitled "Research to Develop Evidence-Based Approaches to Patient Engagement" was approved unanimously.

Patient Engagement for Priority Cancer Sequencing (New RFA/Coop. Agr.)—Dr. Leah Mechanic

Dr. Leah Mechanic, Program Director, DCCPS, presented a new concept on patient engagement for priority cancer sequencing, which is a demonstration project for the Direct Patient Engagement for Discovery Science Research Program. Dr. Mechanic informed members that the goals are to support the targeted direct patient project, generate a comprehensive genomic landscape of cancers that are poorly understood, and address research gaps and NCI priorities. Although the Cancer Genome Atlas (TCGA) has been successful in the general characterizations of cancer, research gaps remain. Regarding the racial and ethnic distribution of TCGA cancers, 14 percent of tumors reflect minority populations and only three percent are representative of the Hispanic population. One approach to address these gaps is the use of a direct patient engagement approach.

This RFA will support cooperative agreements for establishing patient engagement, recruitment, tissue acquisition, data collection, analysis and interpretation, and return of information. Applicants will be asked to develop a patient engagement plan to be evaluated in a peer review process and use state-of-the-art, culturally sensitive, and appropriate methods of engagement.

Subcommittee Review. Dr. Lacey expressed the Subcommittee's appreciation to the NCI for bringing this concept to the forefront. The Subcommittee expressed concern that the concept is broadly defining patient engagement, which would be challenging to a peer review process. The RFA should clearly define which barriers are to be addressed by the applicants.

Questions and Answers

Dr. Ley suggested incorporating Clinical Laboratory Improvement Amendments–approved sequencing tests into the RFA.

The first year cost for the one-time issuance is estimated at \$2.4 M for four U01 awards, with a total cost of \$12 M for 5 years.

Motion. A motion to defer on the DCCPS’ RFA/Coop. Agr. entitled “Patient Engagement for Priority Cancer Sequencing (PE4PC-Seq)” was approved unanimously.

**Portal to Support Patient Engagement Projects (Leidos Contract) (Information Only—
Dr. Hannah Dueck**

Dr. Jaffee introduced the portal to support patient engagement projects, which will be supported by a Leidos contract rather than a grant and was presented as information only and did not require a vote.

Dr. Hannah Dueck, Presidential Management Fellow, NCI, informed members that the portal concept is to support patient engagement projects, is an initiative of the Direct Patient Engagement for Discovery Science Research Program. Dr. Dueck indicated that the aim is to develop a portal and related tools to support NCI projects that directly engage individuals as a part of their research design. Recruitment, enrollment, and information exchange are the types of activities that can be supported through a portal. The Cancer MoonshotSM Biobank and the Rare Tumor Patient Engagement Network are two projects that require a portal by design. This portal project will consist of a patient gateway, which will be hosted by cancer.gov, and modular components (e.g., reusable or customizable modules).

Dr. Dueck explained that the portal project will be developed in two phases. Phase 1—generate recommendations for modular components and launch a gateway—has been approved. The recommendations will be implemented in Phase 2.

XIII. ADJOURNMENT—DRS. ETHAN M. BASCH AND ELIZABETH M. JAFFEE

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

There being no further business, the 11th BSA/NCAB Joint meeting adjourned at 11:12 a.m. on Wednesday, June 27, 2018.

Date

Ethan M. Basch, M.D., M.Sc., Acting Chair, BSA

Date

Elizabeth M. Jaffee, M.D., Chair, NCAB

Date

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