DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
9TH JOINT MEETING OF THE BOARD OF SCIENTIFIC ADVISORS AND THE NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
June 20–21, 2017

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

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
June 20–21, 2017

The Board of Scientific Advisors (BSA) and the National Cancer Advisory Board (NCAB) convened for the 9th Joint Meeting on 20–21 June 2017 in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, 20 June 2017, from 8:30 a.m. to 4:30 p.m., and Wednesday, 21 June 2017, from 9:00 a.m. to 11:12 a.m., and closed to the public on Tuesday, 20 June 2017, from 4:40 p.m. to 5:45 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 the BSA Chair, Dr. Chi V. Dang, Director, Abraham Cancer Center, Professor of Medicine, Perelman School of Medicine, University of Pennsylvania, presided during the open session. Dr. Jaffee presided during the closed session.

BSA Members
Dr. Chi V. Dang (Chair)
Dr. Kenneth C. Anderson (absent)
Dr. Dafna Bar-Sagi
Dr. Ethan M. Basch
Dr. Michael John Becich
Dr. Sangeeta N. Bhatia (absent)
Dr. Melissa L. Bondy*
Dr. Arul M. Chinnaiyan (absent)
Dr. Graham A. Colditz
Dr. Christopher M. Counter
Dr. Joseph M. DeSimone (absent)
Dr. Daniel C. DiMaio (absent)
Dr. Karen M. Emmons
Dr. Carol E. Ferrans
Dr. Chanita A. Hughes-Halbert
Dr. James V. Lacey
Dr. Maria Elena Martinez
Dr. Luis F. Parada
Dr. Sylvia Katina Plevritis (absent)
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
Dr. Ian M. Thompson*
Dr. David A. Tuveson*
Dr. Cheryl L. Walker
Dr. Eileen P. White
Dr. Kevin P. White (absent)
Dr. Cheryl L. Willman*(absent)

* pending appointment

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
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 (absent)
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
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS (absent)
Dr. Richard Pazdur, FDA (absent)
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH
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, 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. Ed Harlow, Special Advisor to the Acting Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Warren Kibbe, Acting Deputy Director and Director, Center for Bioinformatics 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. Jerry Lee, Deputy Director, Center for Strategic Scientific Initiatives
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Ms. Donna Siegle, Acting Executive Officer, 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. Ted 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 Wiltrout, Special Advisor to the Acting Director
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Carolyn Aldige, Prevent Cancer Research 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 Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Dr. Gerald F. Joseph, 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 Shriver, National Coalition for Cancer Survivorship
Ms. Kristy Smith, 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

TABLE OF CONTENTS

TUESDAY, 20 JUNE 2017

WEDNESDAY, 21 JUNE 2017

TUESDAY, 20 JUNE 2017

I. CALL TO ORDER AND OPENING REMARKS—DRS. CHI V. DANG AND ELIZABETH M. JAFFEE

Dr. Elizabeth Jaffee called to order the 9th 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. Chi Dang 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 17 February 2017 NCAB meeting was approved unanimously.

Motion. A motion to approve the minutes of the 21 March 2017 BSA meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DRS. CHI V. DANG AND ELIZABETH M. JAFFEE

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

III. NCI ACTING DIRECTOR'S REPORT—DRS. DOUGLAS R. LOWY, JAMES H. DOROSHOW, WARREN KIBBE, AND DINAH SINGER

Dr. Douglas R. Lowy, Acting Director, NCI, welcomed members of both the NCAB and BSA to the ninth joint meeting of these Boards. Dr. Lowy was joined by Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, who provided an update on NCI's Clinical Research Programs, Dr. Warren Kibbe, Acting Deputy Director, NCI, who updated the attendees on NCI's computational efforts, and Dr. Dinah Singer, Acting Deputy Director, NCI, who provided an update on the Cancer Moonshot℠ implementation plan.

Personnel Changes. Dr. Lowy told members that President Donald J. Trump announced on June 9, 2017, his intent to appoint Dr. Norman E. "Ned" Sharpless, Director, Lineberger Comprehensive Cancer Center, Wellcome Distinguished Professor in Cancer Research, University of North Carolina at Chapel Hill, as Director of the National Cancer Institute. The NCI is looking forward to working with Dr. Sharpless and anticipates that he will be equally successful as the Institute's next director as he has demonstrated in his professional career. Dr. Kibbe, Director, Center for Biomedical Informatics and Information Technology, will join Duke University School of Medicine as chief for Translational Biomedical Informatics in the Department of Biostatistics and Bioinformatics and Chief Data Officer for the Duke Cancer Institute in August 2017. Dr. Lowy expressed appreciation to Dr. Kibbe for his leadership and advice on NCI computational efforts, including NCI–Department of Energy (DOE) collaborations and NCAB Blue Ribbon Panel (BRP) Enhanced Data Sharing Working Group recommendations.

Budget and Appropriations. Members were informed that Congress voted to increase NIH regular appropriations for the second consecutive year, which includes increases for the NCI. The Chairs of the House and Senate Appropriations Subcommittees on Labor, Health and Human Services, Education, and Related Agencies (LHHS)—Oklahoma Representative Thomas Cole and Missouri

Senator Roy Blunt, respectively—remain committed to sustaining increases in regular appropriations for the NIH. The NCI regular appropriations for fiscal years (FYs) 2016–2017 was $400 million (M) higher than that for FY 2014. NCI's FY 2017 appropriations includes a $300 M allocation for the Cancer Moonshot℠ to accelerate research progress; this allotment augments the regular appropriations. Dr. Singer updated the Boards on the proposals and funding opportunity announcements (FOAs) for the Cancer Moonshot later in the meeting.

Research supported by regular appropriations are largely non-overlapping with Cancer Moonshot activities and include training of next-generation researchers, investigator-initiated research, most clinical trials, the Precision Medicine Initiative in Oncology, and the Frederick National Laboratory for Cancer Research (FNLCR)-led RAS Initiative. The NCI relies heavily on the progress that investigator-initiated research affords to cancer research and remains committed to making those investments. For example, Type 1 and Type 2 awards were supported in the amount of $500 M, an increase over the $400 M spent in FY 2013. Again, in FY 2017, the NCI anticipates funding the Noncompeting Continuation (Type 5) awards at 100 percent—a trend seen in FYs 2015 and 2016. The ongoing RAS Initiative underwent an in-depth review by the Frederick National Laboratory Advisory Committee (FNLAC) in November 2016. The FNLAC recommended increased support to continue developing and bring to fruition effective interventions for cancers harboring KRAS driver mutations.

NCI's New Initiatives. Dr. Lowy expressed appreciation to the Boards for their continued support of NCI's programs and updated members on two new initiatives: the National Cryo-Electron Microscopy (cryo-EM) Facility (NCEF) at FNLCR and the Tomosynthesis Mammography Imaging and Screening Trial (TMIST). The NCEF, which leverages the expertise of Dr. Sriram Subramaniam, Senior Investigator, Laboratory of Cell Biology, Center for Cancer Research (CCR), opened in May 2017 as a service facility to assist the structural biology community in solving molecular structures and complexes important to cancer research. The NCI and the FNLAC *Ad Hoc* NCEF Oversight Subcommittee endorses strengthening and deepening the opportunities for the NIH to make progress in cryo-EM as it relates to cancer research.

TMIST, a large randomized controlled trial (RCT), is being conducted in collaboration with the Eastern Cooperative Oncology Group and the American College of Radiology Imaging Network (ECOG-ACRIN) Cancer Research Group. The goal is to determine whether the cumulative rate of advanced breast cancer in women undergoing screening with tomosynthesis plus digital mammography is reduced compared to digital mammography alone. Biannual screening of normal-risk menopausal women, annual screening of menopausal women at increased risk, and establishment of a biorepository are features of TMIST. The NCI anticipates that TMIST will demonstrate that tomosynthesis represents a major advance in mammography that will offer real benefit for women regarding breast cancer screening, which could change the standard of care and result in a one-third lifetime reduction in the number of screening mammograms a woman in the United States undergoes.

Dr. Lowy reminded members of the recent initiative to conduct a four-arm non-inferiority RCT in Costa Rica, which is being undertaken in collaboration with the Bill and Melinda Gates Foundation (Gates Foundation). The trial will determine whether the U.S. Food and Drug Administration (FDA)-approved vaccines Gardasil®9 (Merck) and Cervarix® (GlaxoSmithkine) provide durable protection against cervical cancer in adolescent girls in one- and two-dose regimens. In addition, the NCI–Gates Foundation collaboration will expand to conducting companion trials in the United States and Tanzania and will support the HPV serology standardization project being led by FNLCR. These efforts, if successful, are expected to result in worldwide standardizations for future vaccine trials, foster development of HPV vaccines regionally, lead to an increase in HPV vaccine uptake, and yield significant health care savings in the United States and worldwide.

NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) Trial. Dr. Doroshow informed members that the initial phase of accruals for the NCI-MATCH trial was completed May 22, 2017, which brings to an end the NCI-supported tumor gene sequencing of patient's biopsies. The trial enrolled and tested tumor biopsies from 6,398 patients, of whom 5,482 have received their test results; 983 had gene abnormalities matching an available treatment, and 660 of the 983 had enrolled for treatment. Of the 25 active treatment arms, 50 percent are fully accrued, 25 percent are close to reaching complete accruals, and 25 percent will need additional accrual for rare mutations. The median assay turnaround time was 16 days, and the assay success rate remained high throughout the study, at 94 percent. In addition, the toxicity profiles were acceptable and objective responses (i.e., measurable responses) for the treatment arms are expected to be reported on within the next 12 to 18 months. Unique to the NCI-MATCH trial is the geographical state-by-state enrollment; states with enrollment of more than 30 patients per million population were not the most populous states (e.g., California). Two-thirds of patients enrolled were from community-based centers, primarily because of the efforts of the NCI-designated Cancer Centers and the NCI Community Oncology Research Program (NCORP) sites. Six new treatment arms were added March 13, 2017, and two of those arms have rapidly accrued patients, including arm Z1E, LOXO-101, which is targeting the rare NTRK fusion mutation.

The second phase of the NCI-MATCH trial, the Rare Variant Initiative, was activated at the end of May 2017 to complete accruals of the 25 percent of treatment arms for patients with rare mutations. The NCI and ECOG-ACRIN have worked over the past year to develop a mechanism to leverage the genomic tumor testing ordered by oncologists during routine clinical care of cancer patients at academic cancer centers and community hospitals. Patients with tumor mutations that match the NCI-MATCH trial treatment arms can be referred by their physicians for the trial. Five patients have been enrolled since June 2017, and several academic and commercial groups have shown interest in participating. The NCI is in the process of establishing quality-control procedures to confirm outside-of-the-trial tumor gene sequencing using the NCI-MATCH Assay System.

NCI Patient-Derived Models Repository (PDMR). Members were told that the NCI PDMR went live in May 2017 with 100 models (e.g., cell lines, organoid cultures), including colorectal cancers and soft-tissue sarcomas. Materials and associated data will be made available to the community at minimal cost, but participants must be able to generate the models at their respective institutions. Data including confirmatory patient-derived xenograft (PDX) pathology reports and whole-exome sequencing results can be accessed from the NCI website: pdmr.cancer.gov. Efforts are ongoing to provide DNA, RNA, and tissue lysates for the available models and expand the PDMR to its goal of 1,000 models.

NCI Data Sharing Initiatives. Dr. Kibbe updated members on NCI's data sharing efforts, including the Genomic Data Commons (GDC), Cancer Genomics Cloud Pilots, and the NCI Data Commons. He reflected on his time at the NCI and expressed appreciation to the NCI staff for their support. Aside from co-locating data sets from The Cancer Genome Atlas (TCGA), Therapeutically Applicable Research to Generate Effective Treatments (TARGET), Cancer Target Discovery and Development (CTD^2), and the NCI-MATCH trial, other groups have shown interest in depositing data into the GDC. Foundation Medicine Inc. (FMI) released 18,000 genomic profiles; the Multiple Myeloma Research Foundation (MMRF) released more than 1,000 cases of multiple myeloma (MM) from the Relating Clinical Outcomes in MM to Personal Assessment of Genetic Profile study, commonly known as CoMMpass; and the American Association of Cancer Research (AACR) project Genomics, Evidence, Neoplasia, Information, Exchange (GENIE) just released its first data set to the GDC. These data are available for viewing and downloading from the NCI website. Appropriate security controls and data sharing agreements are in place. In addition, the NCI Cancer Genomics Cloud Pilots are designed to use data from the GDC and are being implemented through commercial cloud providers. The cancer research community will have access to genomics data for analysis without having to perform extensive downloads to a local computer.

The NCI Data Commons framework encompasses, more broadly, other forms of data—including analytical, imaging, clinical, and functional models—and aligns with the Cancer Moonshot data sharing goals and recommendations. The objective is to establish a "data lake" where investigators would have the ability to deposit their data, share it appropriately, and provide the public with access to that data. Furthermore, aligning with the Cancer Moonshot data sharing goals on ways to encourage the cancer community to engage in open access for publications, data, and science initiatives, the NCI will soon be releasing a Cancer Moonshot℠ Open Access Policy. This policy specifies that publications be released after a short embargo period of, ideally, less than 1 month and that the associated data be made available under similar licensing. For example, sequence alignment data files from next-generation sequencing studies resulting from Cancer Moonshot–funded research, as well as data from mass spectrometry analysis or imaging studies, would be shared through the GDC or NCI Data Commons. The NCI anticipates that the Cancer Moonshot Open Access Policy will accelerate progress and science for cancer research.

Cancer Moonshot Recommendations Implementation Plan. Dr. Singer updated members on NCI's implementation plan for the Cancer Moonshot NCAB BRP recommendations. Following the September 2016 BRP Report, NCI identified seven of the 10 recommendations that could be accelerated immediately for FY 2017 and worked expeditiously to transform them into 24 FOAs. Of the 24 FOAs, 15 have closed and nine are still accepting applications. Applications are currently being reviewed and additional details can be accessed from NCI's website. For FY 2018 initiatives, the NCI developed an implementation plan that involves soliciting input from the cancer community in a manner that includes establishing Cancer Moonshot Implementation Teams (CMITs). Twelve CMITs were assembled to focus on two recommendations per team, including demonstration projects; the CMITs, which began conducting weekly meetings in February 2017, are engaging the community via webinars, workshops, or small meetings to discuss the best way to implement the recommendations. A significant number of NCI staff, both intramural and extramural, are invested in the CMITs, which include representatives from other NIH Institutes and Centers (ICs). The nine Cancer Moonshot concepts being presented for the Boards' consideration later in the meeting are a result of these efforts; the concepts were previously vetted through the NCI prioritization process. In addition, three concepts will be funded through the contract mechanism to support three pilot projects in the extramural program; one intramural project will be supported in FY 2018. After implementing FY 2018 initiatives, the NCI will begin to address funding the more complex recommendations for FY 2019. The cross-cutting themes—data sharing through open access and health disparities—will be included in all application templates for the Cancer Moonshot FOAs and Requests for Applications (RFAs). Dr. Singer expressed appreciation to Dr. Lowy for his leadership guiding NCI through major accomplishments during the past 2 years.

Questions and Answers

Ms. Mary Lou Smith, Co-Founder, Research Advocacy Network, asked about the potential for patients to self-refer for the MATCH Rare Variant trial. Dr. Doroshow explained that the NCI has signed agreements with two academic centers and two commercial molecular testing laboratories to provide tumor profiling services. These partnering laboratories will notify the physician who ordered the tumor gene sequencing tests for routine cancer patient care when a specific mutation is a genetic match to any of the MATCH trial treatment arms. The challenge will be to maximize the opportunity for patient access to treatment and access to the MATCH Rare Variant trial by enhancing the ability of patients and their physicians to obtain this information. The NCI welcomes input from the Boards on how best to address this challenge.

Dr. Kevin M. Shannon, Roma and Marvin Auerback Distinguished Professor in Molecular Oncology, American Cancer Society Research Professor, Department of Pediatrics, University of California, San Francisco, pointed out that the MATCH Rare Variant trial, which involves cancer patients

with rare mutations who are geographically dispersed across the United States, would undoubtedly require establishing a National Human Subjects Review Board to address the challenges of conducting these types of trials robustly. Dr. Doroshow explained that additional NCI Precision Medicine Initiative in Oncology (PMI-O) funds have been allocated to expand current pharmaceutical distribution agreements. Dr. Peter C. Adamson, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital in Philadelphia, added that in his experience with conducting pediatric clinical trials (i.e., rare variant-like), a central Institutional Review Board and the necessary infrastructure that allows screening of potential candidates would be essential.

Dr. Dafna Bar-Sagi, Vice Dean for Science, Senior Vice President, and Chief Scientific Officer, Professor, Department of Biochemistry and Molecular Pharmacology, NYU Langone Medical Center, New York University School of Medicine, asked about the mechanisms for soliciting resources for the PDMR given the current landscape of models across the various academic institutions that could be leveraged. Dr. Doroshow replied that the initial 100 models currently available in the PDMR were developed from resources acquired primarily from the NCI-Designated Cancer Centers (Cancer Centers). The NCI is in the process of collecting additional resources from other institutions, and validations against curated models are ongoing.

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 the MATCH trial's capability to perform second biopsies of tumors of patients who are not responding to treatments to better understand the mechanisms of drug resistance. Dr. Doroshow explained that the PMI-O set-aside funds are supporting whole-exome sequencing of tumors from patients enrolled in the MATCH trial treatment arms in addition to the initial screening sequencing analysis. Performing second biopsies in patients whose tumors were refractory to treatment is being supported as well.

Dr. Victoria L. Seewaldt, Ruth Zeigler Professor, Chair, Department of Population Sciences, Beckman Research Institute, City of Hope, commented on NCI's ability to reach across the United States and into other countries and wondered whether there had been outreach efforts to State legislators to increase awareness about how science has impacted their communities. Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences (DCCPS), called attention to the first National Rural Cancer Control Research Conference planned for May 30–31, 2018, on the NIH campus as one example of NCI's efforts to increase community awareness. He noted that other federal agencies, including Health Resources and Services Administration (HRSA) and the Centers for Disease Control and Prevention (CDC), are further along in implementing policies related to rural health, which the NCI is leveraging.

IV. LEGISLATIVE REPORT—M. K. HOLOHAN

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations (OGCR), reported on the budget and appropriations; congressional hearings, briefing, and visits; and other legislation of interest. The President signed the FY 2017 omnibus appropriation bill into law on May 5, 2017, and the NIH received a $2 billion (B) increase, which included the $352 M appropriated in the 21st Century Cures Act. The NCI received a $174 M increase in addition to the $300 M allotted for the Cancer Moonshot that was provided through the December 2016 continuing resolution (CR). On May 23, 2017, the White House Office of Management and Budget (OMB) released the full FY 2018 budget, which includes a 20 percent decrease for the NIH budget compared to FY 2017.

Prior to the release of the President's FY 2018 budget, the NCI attended a House Appropriations Subcommittee on LHHS briefing on May 17, 2017, which focused on the advances in biomedical research. The Subcommittee members spoke positively on the importance of supporting the NIH and

regular increased and sustained appropriations. A Senate LHHS Appropriations Subcommittee budget hearing is scheduled for June 22, 2017; Dr. Francis Collins, NIH Director, will serve as the testifying witness, and he will be accompanied by IC directors, including Dr. Lowy, who will answer questions about cancer research. The NCI/NIH budget process for the regular appropriations is currently at step two of the four-step process. The House and Senate LHHS Appropriations Subcommittees are considering the President's budget proposal and are preparing legislation over the spending bills. Historically, the 12 separate appropriation bills, which are divided by jurisdictions, have been bundled into an omnibus. Some bills continue the prior year's funding level as a CR, whereas others will proceed on a new funding level—when that happens, it is referred to as a "cromnibus." The time to complete the FY 2018 budget is short, with only 13 weeks remaining in FY 2017 and 39 days when both the House and the Senate will be in session. Options for FY 2018 include a 12-bill omnibus, a full-year CR maintaining current funding levels, or a cromnibus. These options are contingent upon absenting new legislation to lift the budget caps to delay sequestration in FY 2018.

Ms. Holohan informed members that congressional bipartisan support for the NIH and the NCI remains strong and extends beyond the appropriations committees. In March 2017, the NCI attended a House Oversight and Government Reform Committee hearing on federally funded cancer research, which was chaired by Utah Representative Jason Chaffetz. Testifying witnesses appearing before the House Oversight Committee included Dr. Mary Beckerle, Chief Executive Officer and Director, Huntsman Cancer Institute, University of Utah; Mrs. Jamie Carr, who had lost a child to cancer; Dr. Tyler Jacks, Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology; and Dr. Jaffee. The hearing was overwhelming positive, and AACR leadership assisted the NCI in preparing the witnesses. Representatives of the House LHHS Subcommittee, which is chaired by Oklahoma Representative Thomas Cole, visited the NIH and the NCI in February 2017 for their annual visit. On April 3, 2017, West Virginia Senator and Senate LHHS appropriator Shelley Moore Capito visited the CCR and met with Dr. Steven Rosenberg and a former immunotherapy patient. For the second consecutive year, the OGCR, in collaboration with NCI's Pediatric Oncology Branch and representatives of the extramural community, hosted members of Congress in May 2017 to learn more about the childhood cancers research effort; representatives from the Department of Health and Human Services (HHS) also attended. On June 5, 2017, nine Senate appropriators, including seven members of the Senate LHHS Subcommittee, chaired by Missouri Senator Roy Blunt, visited the NIH. They toured the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Mental Health. This level of outreach speaks to the commitment and congressional bipartisan support for the NIH and the NCI.

V. RFA/COOP. AGR. CONCEPTS—NEW AND RE-ISSUE—NCI STAFF

Office of the Director

Innovative Molecular Analysis Technologies (IMAT) (Re-Issue RFA) — Dr. Tony Dickherber

Dr. Tony Dickherber, Program Director, Center for Strategic Scientific Initiatives, presented a reissue concept for the IMAT, which was established in 1998 to exclusively support investigator-initiated early-stage technology development that is not addressed in other NIH funding opportunities. The IMAT program is a trans-divisional cooperative initiative in which the exploratory/developmental research award mechanisms (i.e., R21/R33) support two tracks: 1) novel molecular and cellular analysis technologies (MCA) and 2) biospecimen science technologies (BST). The IMAT RFAs continue to receive high-scoring applications focused on cancer-relevant technologies, and exemplify a strong record of success as documented by external program outcome evaluations. For example, the extensive process and impact evaluation conducted in FYs 2015–2016 by Ripple Effect Communications Inc., and

supported by the NIH Office of Program Evaluation and Performance, revealed that 73 percent of the total number of awards accounted for all program publications—a positive indicator that the NCI is achieving a high-risk/high-impact outcome from the management of the IMAT program. There has been a steady accrual in citations associated with these publications, indicating continuous investments in projects that are relevant to the broader cancer research community. To assess the question of how the IMAT program investments matched the accomplishments, Ripple Effect worked with a trans-NIH advisory group consisting of program directors and evaluation experts from other NIH ICs to identify a cohort group that had similar investments as the IMAT grantees. Findings showed that the IMAT group (sample size $n = 540$) published more manuscripts in high-impact peer-reviewed journals per dollar invested when weighted against the comparison group ($n = 473$). The IMAT group also had pursued patent applications for their products at a greater rate per dollar invested than the comparison group. Program evaluations, comments from the BSA, and the NCAB Cancer Moonshot BRP recommendations have informed the latest modifications to the IMAT program.

The reissuance would support four RFAs for innovative early-stage and advanced development and validation of emerging MCA and BST high-risk/high-impact, multidisciplinary cancer-relevant technologies and one RFA to support competitive revisions awards to facilitate incorporation of emerging cancer research technologies. These awards would include 16–19 MCA R21 and 10–12 MCA R33 awards per year; 2-4 BST R21 and 1-2 BST R33 awards per year; and 2-3 competitive revisions 2-year awards (e.g., R01, U01, U54, P01, or P50) beginning in FY 2019.

Subcommittee Review. Dr. Michael John Becich, Pathology Information Sciences/ Telecommunications, Clinical/Translational, Department of Biomedical Informatics, University of Pittsburgh School of Medicine, expressed the Subcommittee's support for the re-issue concept and remarked on the extensive IMAT program evaluation and the definitive data it provided. Dr. Becich noted that the IMAT program has achieved tremendous success and is commendable for its exclusive support of investigator-initiated early-stage technology development. The Subcommittee appreciates NCI staff responses to their questions about the BST and commercialization and is confident that the addition to include competitive revisions awards will be a successful part of the concept reissuance.

The first year cost is estimated at $10.4 M for 35–36 R21 and R33 awards and $0.6 M for two to three R01, U01, U54, P01, or P50 competitive revisions awards, with a total cost of $29–$31 M for 3 years.

Questions and Answers

Dr. Margaret R. Spitz, Professor, Dan L. Duncan Cancer Center, Baylor College of Medicine, wondered whether the IMAT program would be considered a Cancer Moonshot initiative. Dr. Lowy explained that the goal is to not impinge upon ongoing projects supported with regular appropriations, but to integrate and complement some aspects of existing initiatives into the Cancer Moonshot. Dr. Singer added that the IMAT RFA is focused on early and emerging technologies, whereas the Cancer Moonshot will primarily focus on accelerating existing technologies.

Dr. Wicha asked about the mechanism for publicizing to the broader community the successful IMAT technologies. Dr. Dickherber explained that the NCI relies heavily on the trans-divisional structure of the IMAT program, including the program directors, to facilitate those connections. The addition of the competitive revisions awards is expected to incentivize collaboration between technology developers and users.

Motion. A motion to concur on the Office of the Director's (OD's) re-issue RFA entitled "Innovative Molecular Analysis (IMAT)" was approved unanimously.

Minority-Patient Derived Xenograft Development and Trial Center (PDTC) Network (New RFA/Coop. Agr.)—Dr. Tiffany Wallace

Dr. Tiffany Wallace, Program Director, Center to Reduce Cancer Health Disparities (CRCHD), presented a new concept to establish a minority PDTC (M-PDTC) Network, which is companion to RFA-CA-17-003, which supports developing a PDTC Research Network (PDXNet) and RFA-CA-17-004, which supports the NCI Patient-Derived Models Repository (PDMR) and the PDX Data Commons and Coordinating Center (PDCCC). Supporting evidence—such as racial disparities in treatment outcomes, differences in drug-metabolizing enzymes, and response to therapies—indicates that disparities in therapeutic outcomes exist among racial/ethnic minority populations. Furthermore, the diversity of public/private/academic repositories—including The Jackson Laboratory, Cancer Genome Atlis (TCGA), and the PDMR—historically has been low. This RFA will establish a M-PDTC Network that will expand the goals of the PDXNet to increase diversity in preclinical models, improve investigator expertise in cancer health disparities (CHD), and strengthen links and infrastructure within communities. In addition, studies within the Experimental Therapeutics Clinical Trials Network (ETCTN) will be better equipped to focus on minority populations and extramural CHD research.

Subcommittee Review. Dr. Carol E. Ferrans, Professor and Associate Dean for Research, Director, University of Illinois at Chicago (UIC) Center of Excellence in Eliminating Health Disparities, Department of Biobehavorial Health Sciences, College of Nursing, UIC, expressed the Subcommittee's strong enthusiasm and support for the concept. Dr. Ferrans stated that establishing an M-PDTC Network is well justified and will advance CHD research. Also, the Network will provide an opportunity to engage new centers and expand the investigator pool for CHD research. She noted that the Subcommittee recommended including language in the RFA to ensure that multiple racial/ethnic groups are represented in the applications selected for funding. Additionally, the NCI should consider developing sustainable measures to address diverse population representations early in the development of CHD-related RFAs.

The first year cost is estimated at $3 M for two U54 awards, with a total cost of $15 M for 5 years.

Questions and Answers

In response to members' comments on the low percentage of minority representation in the PDMR, Dr. Wallace explained that data collection on ancestral formative markers will be standard within the PDMR. Dr. Doroshow also noted that retrospectively collecting data on models whose racial/ethnic backgrounds had not been indicated revealed a 10 percent diversity in the PDMR. Dr. Seewaldt suggested including representations from mixed-race populations.

Dr. Judy E. Garber, Director, Center for Cancer Genetics and Prevention, Dana Farber Cancer Institute, Professor of Medicine, Harvard Medical School, pointed out that successful applications are likely to attract collaborators who would be willing to increase diversity in PDX models at their respective institutions and noted that additional funding may be needed to support any new collaborative efforts or programs to meet the challenge of establishing M-PDTCs and succeeding in commercialization.

Dr. Dang asked about the standard operating procedures (SOPs) that govern acquisition, storage, and dissemination of PDX models at the different sites and wondered whether the Frederick National Laboratory for Cancer Research (FNLCR) could play a role in conducting preclinical studies to ensure uniformity in the PDTCs. Dr. Doroshow referred members to the PDMR website (pdmr.cancer.gov) for details on SOPs and noted that applications currently are being reviewed to support development, characterization, and usage for the PDXNet.

Dr. David A. Tuveson, Professor and Deputy Director, Cancer Center, Cold Spring Harbor Laboratory, expressed concern that the efforts to generate PDX models from disparate ethnic groups in different or contrasting cancer types will be statistically underpowered to make scientific conclusions and encouraged the NCI to consider rigorously performing germline, as well as somatic, sequencing to firmly identify genetic differences at the molecular level. Dr. Lowy agreed that extensive genomic analysis of patient samples from underrepresented minorities should be a priority and called attention to NCI's efforts, the Early Onset Malignancy Initiative, organized through the NCI Community Oncology Research Program (NCORP), which will develop the first minority-based cancer tissue bank of early-onset tumors and will collect information on treatment, response, and outcome.

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, remarked that one way to address CHD would be to focus on the educational, political, and social causes of health disparities, as well as diversity in investigators and institutions conducting health disparities research, rather than focusing exclusively on genetic differences. Dr. Lowy conveyed NCI's sentiment that that both health care access and utilization and diversity in research and among research investigators are important. He noted that the NCI has focused this RFA on areas that will impact the research by exploring the biological opportunities to investigate racial/ethnic differences in cancer. Other groups that focus on the sociological aspects of health disparities could be engaged to lead those efforts.

In response to a query from Dr. Wicha on capturing data on African populations, Dr. Lowy replied that capturing those data was beyond the scope of this RFA and noted that the NCI welcomes clinically annotated PDX models from African population specimens that could be made available to the research community.

Dr. Cheryl L. Walker, Professor and Director, Institute of Biosciences and Technology, Center for Translational Cancer Research, Welch Chair in Chemistry, Texas A&M Health Science Center, inquired about collecting information on patient's environmental exposure for the PDMR. Dr. Yvonne Evrard, Operations Manager, Leidos Biomedical Research, Inc., explained that data on a patient's occupation, as well as speculative cancer-related causative exposures, are requested for the PDMR database, but they may not be captured at all participating sites.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Minority-Patient Derived Xenograft (PDX) Development and Trial Center (PDTC) Network" was approved unanimously.

Investigation of the Transmission of Kaposi Sarcoma–Associated Herpesvirus (KSHV) (New RFA) —Dr. Rebecca Liddell Huppi

Dr. Rebecca Liddell Huppi, Program Director, Office of HIV and AIDS Malignancy (OHAM), presented a proposal to investigate the transmission of KSHV (i.e., human herpesvirus-8). The concept was proposed in collaboration with the Division of Cancer Prevention (DCP), DCCPS, the Division of Cancer Biology (DCB), and the National Institute of Dental and Craniofacial Research (NIDCR). Of the estimated 2.1 million new HIV infections being diagnosed annually, 90 percent occur in low- to middle-income countries (LMIC), and 70 percent of these occur in sub-Saharan Africa. Kaposi Sarcoma (KS), one of three principal tumors caused by KSHV, is one of the most common HIV-associated malignancies worldwide, with approximately 44,000 new cases being reported annually, and is the most common HIV-associated malignancy in sub-Saharan Africa. Although HIV is better controlled with the advent of

effective therapies, including highly active antiretroviral therapy (HAART), which also decreased and then stabilized the incidence of KS in the United States and other developed countries, KS remains one of the most common HIV-associated malignancies, even when HIV is well controlled. Furthermore, there is concern that as the HIV-infected population ages, KS will reemerge. The predominant modes of KSHV transmission and associated risk factors for infection are not well understood and are thought to vary by country. In endemic areas, such as sub-Saharan Africa, much of the acquisition is thought to occur from childhood saliva exchange. In non-endemic areas, sexual transmission appears to be the primary route of exposure. Preventing the spread of KSHV would prevent the development of KS and other KSHV-related diseases, but the uncertainty regarding the principal routes of exposure, the lack of a Food and Drug Administration (FDA)-approved gold standard serological assay, and lack of a suitable vaccine are hindering progress. Thus, the intent of this RFA concept is to prevent KSHV infection, KS, and other KSHV-induced diseases in populations living with HIV or those at high risk for developing HIV. The RFA concept aligns with the 2013 recommendations of the BSA a*d hoc* Subcommittee on HIV and AIDS Malignancy.

The RFA would support awards to increase understanding of the modes of transmission of KSHV that could potentially inform public health measures to prevent the spread of KSHV. The NCI-appropriated AIDS funds, as established by the NIH Office of AIDS Research, will support this research.

Subcommittee Review. Dr. Seewaldt expressed the Subcommittee's strong support for this research to address the important topic of KSHV transmission in endemic regions, which would extend to non-endemic regions. She noted that the Subcommittee voiced reservations about the scope and implementation science and recommended revising the KSHV concept to include a clearer focus of the priorities and deliverables necessary to meet the goals of the RFA and to clarify the implementation strategies for behavioral interventions, particularly in sub-Saharan Africa, regarding modes of transmission and the details of cell biology to be addressed.

The first year cost is estimated at $4.5 M for 8 to 10 R01 and R21 awards, with a total cost of $22.5 M for 5 years.

Questions and Answers

Dr. 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, commended the NCI for addressing a global problem with research that is long overdue. Dr. Gostin observed that vaccine research was not being prioritized and encouraged the NCI to develop strategies for conducting clinical trials in sub-Saharan Africa.

Dr. Yuan Chang, American Cancer Society Research Professor, Distinguished Professor of Pathology, University of Pittsburgh Cancer Institute (UPCI), and Chair of Cancer Virology, UPCI, noted the research advances for KSHV that have enabled the field to reach this current inflection point and encouraged the NCI to support initiatives to develop a vaccine. Dr. Huppi commented that the OHAM anticipates that this RFA could provide the necessary groundwork on the mode of transmissions that would inform future vaccine development. Dr. Robert Yarchoan, Director, OHAM, acknowledged the comments of the Boards and reflected on the 2013 BSA a*d hoc* Subcommittee on HIV and AIDS Malignancy recommendation to learn more about KSHV transmission and to consider developing appropriate guidelines to prevent KSHV transmission, which did not include an immediate path to pursue vaccine development. Dr. Yarchoan informed the Boards that the a*d hoc* Subcommittee will reconvene on 21 June 2017 and will further discuss the topic. Dr. Lowy stated that the NCI, in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), is supporting development of an Epstein-

Barr Virus vaccine that, if it progresses, will be the first successful herpes vaccine. Whether those same principles would apply to a KSHV vaccine remains to seen.

Motion. A motion to defer the OD's RFA/Coop. Agr. entitled "Investigation of the Transmission of Kaposi Sarcoma-Associated Herpesvirus (KSHV)" was approved with 18 ayes, 0 nays, and 2 abstentions.

VI. ENHANCING STEWARDSHIP: NEXT GENERATION OF RESEARCHERS INITIATIVE—DRS. L. MICHELLE BENNETT AND LAWRENCE TABAK

Dr. Lawrence Tabak, Deputy Director, NIH, updated members on the Next Generation of Researchers Initiative (Initiative), which is aligned with the objectives of the NIH-Wide Strategic Plan and the 21st Century Cures Act per *Subtitle C, Section 2021*. Many in the extramural community have made observations similar to those reflected in the 2014 report titled "Rescuing U.S. Biomedical Research from its Systemic Flaws," which identifies an "unsustainable hypercompetitive" system as the cause of discouragement for promising scientists wanting to enter the biomedical fields, which the report indicates was due to an over-exaggerated assumption that the rapid growth in biomedical sciences will never come to an end. The NIH recognized that the current environment is dissuading younger scientists and investigators from entering biomedicine and emphasizes the need to address this issue. The Office of Extramural Research and the Statistical Analysis and Reporting Branch reviewed the landscape of applicants and awardees in the Research Project Grant (RPG) program (i.e., R01) from FY 2003 to FY 2015 to evaluate the hyper-competitiveness and, unsurprisingly, while the number of applicants steadily increased, the number of awardees remained constant. Stratifying by age, the number of funded investigators older than 60 years of age started to increase in FY 2000 and continues to rise today, whereas the number of early-stage funded investigators (i.e., 45 years or younger) has been rapidly declining, that is, until NIH implemented the New and Early-Stage Investigator (ESI) Policy in 2008. The number of mid-career level funded investigators (i.e., 46 to 60 years of age) started to decline after having experienced a long period of rising numbers. Multiple analyses indicated that established principal investigators are outcompeting ESIs and mid-career investigators; the resiliency to resubmit a revised application is likely to favor established researchers, who often have additional funding sources.

Although the ESI Policy has had a positive and stabilizing effect, it has not achieved the full benefit of the declining trend in ESIs. The goal for the NIH is to determine ways to increase the number of funded early-career scientists and stabilize the career trajectories of all scientists. Despite successful efforts to enhance the prioritization of ESIs, in FY 2016 across the NIH, 193 R01 applications from ESIs that scored in either the 25th percentile or lower or had priority scores of 35 or less were not funded. The NIH is proposing to extend the payline for ESIs. In addition, despite ongoing efforts to provide new support systems to nurture investigators with less than 10 years of experience who just missed funding in the competitive renewal process, 263 R01 applications from mid-career level investigators in the same scoring category as ESIs were not funded in FY 2016. Furthermore, in FY 2016, 75 R01 applications from mid-career investigators who successfully renewed their R01s and were seeking support for a second R01 to build up resiliency were not funded. The NIH proposes to prioritize support for mid-career level investigators who are on the verge of losing NIH funding and are likely to leave the biomedical workforce, and it will rely on its program staff to continue to identify "rising stars" and prioritize support for those seeking a second R01 that could stabilize and sustain their career paths.

Dr. Tabak informed members that under the new NIH proposed plan, the ICs have committed to ensuring support for highly meritorious ESIs and mid-career level investigators. Starting immediately, the NIH OD will generate an inventory of such investigators whose applications are within the fundable range, track IC funding decisions for this pool, and evaluate the uniformity of the decision-making process across the NIH. Based on the FY 2016 numbers of potential fundable investigators in the 25th percentile range, the NIH estimates requiring $210 M per year to fund these additional investigators in the

first year, with a total cost of $1.1 B for 5 years. The implementation of the new proposed plan will require a reprioritization of funds within the different funding mechanisms across the ICs that are currently being used to build in resiliency (e.g., R56, R35, or supplements). Aligning with the objectives of the NIH-Wide Strategic Plan to optimize approaches to *inform* funding decisions, the NIH leadership will assume this role, but the funding decisions will remain under the purview of the IC Directors.

Assessing the impact of NIH research requires developing metrics of productivity. In the long term, the goal would be to assess the value of NIH investments by measuring outcomes, including disruptions in prevailing paradigms in biomedicine, development of new technologies, or improvements in public health. Good stewardship also requires strategies to assess impact in the short term, which speaks to establishing a reliable approach to measure the interim influence of NIH funding. Short-term assessments will require validated metrics for productivity and metrics for grant support that are based on commitment rather than dollar amount. NIH has developed and validated the Relative Citation Ratio (RCR) bibliometric tool to assess the influence of publications in PubMed and has launched a publicly available dashboard of bibliometrics, iCite (icite.od.nih.gov). Work is ongoing to develop and refine grant support metrics. However, beginning immediately, NIH is committed to redistributing ~$1.1 billion, over the course of 5 years, to support additional meritorious and mid-career investigators. Dr. Tabak expressed appreciation to the many stakeholders for their comments on ways to strengthen the biomedical workforce and conveyed NIH's commitment to reprioritize the necessary funds to support additional meritorious research from early- and mid-career investigators. The NIH will encourage independent analyses of metrics that can be used to assess the impact of the NIH portfolio. All actions will continue to be informed by stakeholder input.

Dr. L. Michelle Bennett, Director, Center for Research Strategy (CRS), NCI discussed the analysis of the productivity trends for NCI-funded investigators; the funding climate for early-, mid-, and late-career NCI-funded investigators; and the NCI R01 turnover rate. The CRS assessed the research productivity of NCI-funded investigators using the same approach described in the report titled "Marginal Returns and Levels of Research Grant Support Among Scientists Supported by the National Institutes of Health," which uses the RCR, the NIH Grant Support Index (GSI) point value for RPGs, and the R software package for statistical computation. Evaluation of 14,000 scientists receiving NCI RPGs from 1996 to 2014 suggest that productivity increases with each increment of GSI. Modifying this approach and using different assumptions, CRS assessed bibliometric productivity as a function of the number of NCI R01s per investigator, and showed that for investigators funded in FY 2011, the number of publications and citations increase with the number of NCI R01s per investigator. Assessing funding trends over time, from 1990 to 2015, by age of NCI RPG investigator in 5-year intervals revealed that the number of funded investigators increased in all age groups except for ESI younger than 40 years of age. In addition, the turnover of NCI R01s is greater than non-NCI R01s on average over the past 3 years for new (Type 1) and competing (Type 2) awards. The NCI recognizes that bibliometrics do not capture the impact of the full breadth of NCI-funded research and that linking a publication to a grant or investigator has a number of challenges.

The Policy supporting the Next Generation Researchers Initiative (NOT-OD-17-101) was released on August 31, 2017. Information on the Policy and the Initiative can be found on the Next Generation Researchers Initiative website (https://grants.nih.gov/ngri.htm).

Questions and Answers

Dr. Shannon suggested analyzing physician-scientists separately from other NCI-funded early- and mid-career investigators in future analyses, because the solutions to their funding issues may be different. He also noted that the time to a first R01 could be related to the requirements of the NCI Mentored Clinical Scientist Research Career Development Award (K08), which requires applicants to

have first-author publications within their postdoctoral positions before their grants are evaluated in study section.

In response to a query from Dr. Adamson on the statistical method used to inform the conclusion that the productivity of NCI investigators increases with the number of R01s, Dr. Melissa Antman, Senior Scientific Program Analyst, CRS, acknowledged that the propagation of error would be large and thus these data were not tested for statistical significance, but they indicate a trend while using methods similar to those used in other NIH presentations. The NCI results suggest that as the number of R01s increase per investigator, the number of publications and citations increased.

Dr. James V. Lacey, Jr., Director and Professor, Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute, City of Hope, asked whether the strategy is to address the barriers in the peer-review process that ESI applications may be disproportionately experiencing or to review and address the science of unfunded applications. Dr. Tabak explained that applications in the 25th percentile will be the focus and that merit review is one important component to making final decisions on funding at the NIH. The NIH Advisory Committee's decisions and scientific and workforce portfolio balancing are also components. Dr. Lowy added that the NCI uses the select pay funding policy for ESIs and noted that the NIH is proposing that it continue, but more extensively.

Dr. Scott W. Hiebert, Hortense B. Ingram Chair in Cancer Research, Professor of Biochemistry, Department of Biochemistry, Vanderbilt University School of Medicine, asked about the ESI funding target rate. Dr. Tabak explained that the NIH projections based on the graph depicting investigators funded stratified by age were informed by the labor economist model of projections for resource shifting and reprioritizations of funds. The balancing will be realized as the number of funded established investigators reaches a plateau, the number of funded mid-career investigators increases slightly to a stable level, and the number of funded ESIs remains stable or even increases slightly.

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 at Chapel Hill, asked about the potential for bridging funding between career development awards and R01s and the support for mentors to assist junior investigators reach their goals. Dr. Tabak replied that many ICs use the R56 funding mechanism for this purpose. Team science can be strategic in some settings regarding mentorship, but also can be a hindrance to a scientist's independence. Dr. Bennett added that team science provides opportunities for junior level scientists to assume leadership roles in research teams to address complex scientific problems that often result in independence through the development of new research projects.

Dr. Roach speculated on the unintended consequences of reduced mentoring for early-career scientists from established investigators if funds are reprioritized unevenly. Dr. Tabak explained that there is no select formula for balancing funds. The NIH is aiming for stabilization across career stages with evidence of increase for ESIs. The hope is to attract the attention of labor economists to provide additional insight and quantitative modeling. The IC directors will review individual applications and decide whether these can be supported on select pay funding, which will require in-depth analysis of the IC's programs.

In response to a query from Dr. Timothy Ley, Professor of Medicine and Genetics, Division of Oncology, Department of Medicine, Washington University School of Medicine at St. Louis, on the efforts to improve stakeholder input, Dr. Tabak responded that stakeholder input has been significant. The next steps will be to establish a formal working group of the Advisory Committee to the Director (ACD) to review future analysis and new approaches.

Dr. Melissa L. Bondy, Professor and Associate Director, Department of Medicine, Dan L. Duncan Cancer Center, Baylor College of Medicine, commended the NIH for developing the metrics and measures of productivity. She suggested that the NIH consider focusing on the gender of ESIs and their funding trajectories. Dr. Tabak pointed out that as the NIH makes funds available to support additional ESIs and mid-career investigators, the expectation is that individuals not yet receiving funding will have a greater opportunity to be supported. Dr. Seewaldt suggested that a mechanism for supplemental salary support for M.D. investigators be considered.

VII. RFA/COOP. AGR. CONCEPTS—NEW AND RE-ISSUES—NCI STAFF

Division of Cancer Treatment and Diagnosis

NCI Clinical Trials Network (NCTN) (Re-issue RFA/Coop. Agr.) — Subcommittee

Subcommittee Review. Dr. Becich expressed the Subcommittee's enthusiasm and strong support for reissuance of the concept. He noted that the role of the NCTN in accruing patients for clinical trials across the NIH is critical. The Subcommittee suggested increasing funding to support improvements and other activities, including the addition of patient-reported outcomes, conducting precision medicine–based clinical trials, and increases in per-case reimbursements.

The first year cost is estimated at $171 M for 49 to 55 awards, with a total cost of $1.026 B for 6 years.

Questions and Answers

Dr. Doroshow expressed appreciation to the Subcommittee for reviewing the concept reissuance and reflected on the history of the NCTN. He stated that the reissuance concurrence today will return the Network to its original funding level, which was disrupted during the 2011 Federal budget sequestration.

Motion. A motion to concur on the Division of Cancer Treatment and Diagnosis' (DCTD's) re-issue RFA/Coop. Agr. entitled "NCI Clinical Trials Network (NCTN)" was approved unanimously.

Office of the Director

Feasibility and Planning Studies (P20) for Development of Specialized Programs of Research Excellence (SPOREs) to Investigate Cancer Health Disparities (New RFA)— Dr. Tiffany Wallace

Dr. Wallace informed members that the concept on the feasibility and planning studies (P20) for development of SPOREs to investigate CHD was being proposed in collaboration with the Translational Research Program, DTCD. She noted that SPOREs are large multicomponent grants that focus on translational research, including organ-specific cancers, a group of highly related cancers, cancers related by common biological pathway mutations, or cross-cutting themes such as CHD. No active SPOREs specifically focus on CHD, and only a limited number address individual disparity-related projects. The majority of the NCI CHD active grants focus on basic biology or population science, not necessarily translational research. As such the CRCHD convened a CHD Research Program Project (P01)/SPORE Development Workshop in parallel to the 2016 American Association for Cancer Research (AACR) CHD conference to address this gap. Interest in developing SPOREs to investigate CHD was realized, and the development of a P20 funding opportunity announcement should be beneficial to support CHD SPOREs

(P20), each containing a minimum of two translational research projects with a proposed human endpoint, two or more independent investigators, a developmental research program, an administrative core with an external advisory board, and a biospecimen/pathology shared resource core would be beneficial. All applications must provide, in detail, a clear transition plan for how the program will evolve into a P50 SPORE within the 3-year funding period.

Subcommittee Review. Dr. Chanita Hughes-Halbert, Professor and Endowed Chair, Department of Psychiatry and Behavioral Sciences, Hollings Cancer Center, Medical University of South Carolina, expressed the Subcommittee's enthusiasm and strong support for the concept. Dr. Hughes-Halbert noted that establishing SPOREs that focus on CHD addresses an important need identified by the scientific community and is responsive to the concerns and priorities of potential applicants. The Subcommittee recommends increasing the number of P20 awards to provide a foundation for full-scale P50 SPORE grants in CHD and leveraging priorities of the Cancer Moonshot initiatives.

The first year cost is estimated at $3.9 M for three P20 awards, with a total cost of $11.7 M for 3 years.

Questions and Answers

Dr. Maria Elena Martinez, Professor, Department of Family Medicine and Public Health, Program Leader, Reducing Cancer Health Disparities, Moores Cancer Center, Sam M. Walton Endowed Chair for Cancer Research, University of California at San Diego, sought clarity on progressing from a P20 to a P50 CHD SPORE. Dr. Hughes-Halbert clarified that a P20 CHD SPORE award would not be a requirement for submitting a P50 application focusing on CHD.

In response to a query from Dr. Ley on the potential for extending P20 awardee meeting invitations, Dr. Wallace replied that the Translational Research Branch would have input on organizing this type of a meeting and could consider inviting potential P20 applicants to future meetings.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Feasibility and Planning Studies (P20) for Development of Specialized Programs of Research Excellence (SPOREs) to Investigate Cancer Health Disparities" was approved unanimously.

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

Office of the Director

Assessing the Tolerability of Anti-Cancer Treatment Using Clinician- and Patient-Reported Outcomes: Methods for Analyzing and Interpreting CTCAE and PRO-CTCAE™ Data (New RFA/Coop. Agr.)—Dr. Ann M. O'Mara

Dr. Ann M. O'Mara, Program Director, DCP, presented a concept to assess the tolerability of anti-cancer treatment using Clinical Terminology Criteria for Adverse Events (CTCAE) and the NCI patient-reported outcome CTCAE (PRO-CTCAE™) methods. Dr. O'Mara stated that the CTCAE is a clinician-rated library of more than 800 adverse event (AE) items with built-in grading criteria for reporting. The AE grading is used in a protocol-specific manner for early- and late-phase clinical trials to identify the maximum tolerated dose, safety assessment, and risk to benefit compared to a standard regimen. Yet, the CTCAE does not provide a comprehensive understanding of the toxicities that cancer patients endure in clinical trials. For example, the time profile of AEs is not accounted for, the impact of chronic and low-grade toxicity on the ability of patients to continue treatment is not captured, and patient-reported

outcomes (PRO) are not incorporated. The NCI PRO-CTCAE™, an Item Library of 78 AE items derived from the CTCAE, was designed to systematically and prospectively capture symptomatic AE and address the gaps in understanding patient tolerance of anti-cancer treatment.

The goals of the RFA are to stimulate development of methods for analyzing PRO-CTCAE™ data in the clinical trial setting, as well as other clinical relevant data to determine the tolerability of anti-cancer treatment and to establish a consortium of funded investigators to share analytical approaches. The RFA would support development of a consortium (U01) and four to six funded teams of statisticians, cancer clinical trialists, and PRO investigators teams.

Subcommittee Review. Dr. Basch expressed the Subcommittee's support for the concept. He noted that the NCI PRO-CTCAE™ is an indispensable patient-centered tool that captures direct experiences and symptomatic toxicities in clinical trials. The Subcommittee voiced concern on whether the RFA would accelerate the use of the PRO-CTCAE™ tool in clinical trials and recommended including an implementation science component, providing more clarity on the main priority for establishing the consortium, and developing a white paper guidance document that would be updateable during the project.

The first year cost is estimated at $3.25 M for three to four awards, with a total cost of $16.25 M for 5 years.

Questions and Answers

In response to queries about the potential to collect data over time on responses to questions on chemotherapy side effects, the impacts of cancer on employment, and the period for collecting data, Dr. O'Mara responded that the PRO-CTCAE™ data are expected to provide more insight into the trajectory of toxicity in the AE time profiles. Input on the period for collecting data will come from the investigators. It is reasonable to expect that a 26-week period would be adequate to capture new AE from immunotherapies.

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, asked about the benefit of limiting the data evaluation to completed/closed trials and suggested prospectively performing data evaluations on open trials. Dr. O'Mara indicated that the 5-year period may be too short for data collection from completed trials and performing analysis on the active trials. The RFA will focus on the analytical techniques that can be used to analyze the data. Dr. Ferrans observed that the data security within the NCTN might restrict collecting PRO-CTCAE™ data. Dr. Lori Minasian, Deputy Director, DCP, explained that other academic institutions have incorporated PRO-CTCAE™ into their Phase I trials and that the RFA will not be limited to NCTN trials. Interest is expected to expand beyond the funding opportunity limits.

Members suggested that the NCI consider revising the terms of agreement for using PRO-CTCAE™ and pursue other options for NCI staff to interact with industry partners and FDA regulators.

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, noted that the Cancer Moonshot recommendations' cross-cutting theme of health disparities should be included the RFA.

Motion. A motion to concur on the Office of the Director's (OD's) Moonshot RFA/Coop. Agr concept entitled "Assessing the Tolerability of Anti-Cancer Treatment Using Clinician and Patient-Reported

Outcomes: Methods for Analyzing and Interpreting CTCAE and PRO-CTCAE™ Data" was unanimously approved with the recommendation that consideration be given to: 1) including approaches for implementation science (specific goals, benchmarks, etc.) and plans for dissemination of standards that could parlay into development of a consensus document (e.g., a White Paper); 2) development of a mechanism to identify key questions; 3) the inclusion of key stakeholders in the advisory board; 4) providing an option for prospective data collection by consortium investigators; 5) assure that innovation simultaneously occurs through users of the tool by industry and the NCTN (formerly cooperative groups).

Collaborative Research Network for Fusion Oncoproteins in Childhood Cancers (New RFA/Coop. Agr.)—Dr. Keren L. Witkin

Dr. Keren L. Witkin, Program Director, DCP, informed members that the concept is to establish a collaborative research network to investigate fusion oncoproteins in childhood cancers. Dr. Witkin stated that recognizing that fusion oncoproteins are well-credentialed oncogenic drivers of high-risk pediatric cancer, including those with no promising targeted treatment options (e.g., Ewing sarcoma, Alveolar rhabdoyosarcoma, Synovial sarcoma, NUP98-fusion leukemias, and RELA-fusion ependyoma), the Pediatric Cancer Working Group of the NCAB BRP identified this as a priority area for cancer research acceleration. A multidisciplinary, collaborative, and comprehensive approach to studying fusion oncoproteins involving structure function data, target identification, small-molecule inhibition, and therapeutic testing is being proposed. This research will complement other NCI funding opportunities: Research Answers to NCI's Pediatric Provocative Questions (PA-16-217/PA-16-218), Gene Fusions in Pediatric Sarcomas (PA-16-251/PA-16-252), and Administrative Supplements to Promote Research Collaborations on Fusion Oncoproteins as Drivers of Childhood Cancer (PA-17-138).

The intent of this RFA is to support three to four Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortiums (U54) of multidisciplinary and multi-institutional collaborative teams focusing comprehensively to better understand the biology of fusion oncoproteins and developing effective therapeutics. Each team or center will focus on a single fusion oncoprotein, and the overall program will be limited to a few high-risk fusion-driven cancers currently lacking effective treatments.

Subcommittee Review. Dr. Shannon expressed the Subcommittee's support for the concept. The Subcommittee encouraged incentivizing multi-institutional collaborations to engage the scientific experts dispersed across the community.

The first year cost is estimated at $7 M for three to four U54 awards, with a total cost of $35 M for 5 years.

Questions and Answers

Dr. Adamson observed that immunotherapy approaches were not included in the RFA, and Dr. Wicha commented on the prescriptive language of the RFA, which is limiting the freedom to select other targets. Dr. Shannon explained that the childhood tumors being investigated are not expected to be immunogenic because of the low mutation rates. This concept is a concerted effort to collectively engage the fusion oncoproteins transcription factor experts. The R01 funding mechanism would be more suited for investigators with innovative ideas on different approaches for investigating fusion oncoproteins in childhood cancers.

In response to a concern expressed by Dr. Hiebert that the research would take longer than the funding period to complete, Dr. Dang remarked on the unmet need being addressed. Dr. Shannon added that the potential to identify new targets within the 5-year period would a reasonable assumption.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Collaborative Research Network for Fusion Oncoproteins in Childhood Cancers" was approved unanimously.

Immuno-Oncology Translational Network (IOTN) (New RFA/Coop. Agr.)—
Dr. T. Kelvin Howcroft

Dr. T. Kevin Howcroft, Chief, Cancer Immunology, Hematology and Etiology Branch, DCB, presented a concept to establish an immuno-oncology translational network (IOTN) to foster collaborative approaches enabling rapid translation of discoveries to clinical application. The IOTN will consist of two components: a Cancer Immunotherapy Consortium (CIC) that will generate organ site–specific sub-networks to develop improved tumor-specific immunotherapy approaches and a Cell Therapy Data Registry and Biorepository to accelerate optimization of cell-based immunotherapies. The CIC will be supported by a Data Management and Resource Center (DMRC) and will include immunoprevention and partnerships sub-networks. This RFA will leverage existing NCI initiatives, including current Cancer Moonshot initiatives (e.g., RFA-CA-17-015), the Cancer Immunologic Data Commons, and the Center for International Blood and Marrow Transplant Research (CIBMTR).

The RFA would support 10 to 12 CIC sub-networks (U01); one DMRC (U24) that will include a network coordinating center, a resource sharing center, and a data sharing center; and one Cell Therapy Data Registry and Biorepository (U24) to collect baseline patient data, treatment outcome data, long-term follow-up reports, and tumor biopsies.

Subcommittee Review. 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 Cancer Center, expressed the Subcommittee's support for the concept. Dr. Parada commended the NCI for including the immunoprevention sub-network that will address early detection and the partnerships sub-network, a mechanism for collaboration with R01 investigators. The Subcommittee noted the applicability of using animal models for studying the underlying biology and suggested assessing AE across the studies/centers.

The first year cost is estimated at $13 M for 10 to 12 U01 awards and two U24 awards, with a total cost of $65 M for 5 years.

Questions and Answers

Dr. Becich inquired as to how the biorepository and data registry would support the NCTN. Dr. Howcroft informed members that the intent is to collect types of data that are not supported by other cell-based therapy initiatives. Dr. Becich suggested leveraging existing NIH open data sharing initiatives, including NIAID's Data Sharing Repositoring, Immunology Database and Analysis Portal (ImmPORT)

Dr. Jaffee asked about the integration of the different groups and disciplines in the network and expressed concern that the funding would not be adequate to support multi-investigator efforts and use of expensive developmental technologies such as T-cell receptor sequencing. Dr. Howcroft stated that there are opportunities for collaboration within the CIC sub-networks that could enable access to resources and the potential to interact with technology support groups to address new technology issues, including cost. Dr. Singer added that providing core resources would be an option to consider. Dr. Jaffee also asked about the role of the Cancer Immunotherapy Trials Network (CITN). Dr. Howcroft explained that members of the Adult Immunotherapy CMIT are coordinators for the CITN and would the best ones to engage that network.

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, commented on the benefits of leveraging the immuno-oncology research expertise in the private sector, where the investments are significant. Dr. Lowy noted upcoming efforts that would complement NCI's initiatives, including the Partnership to Accelerate Cancer Therapies (PACT), a soon-to-be-established public-private partnership for immunotherapy biomarker development and the Cancer Immune Monitoring and Analysis Centers (CIMACs), which supports immunotherapy trials. Dr. Singer added that the Cancer Moonshot Implementation Partnership Committee will begin to engage potential partners as the RFAs progress.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Immuno-Oncology Translational Network (IOTN)" was approved unanimously.

Human Tumor Atlas Network (New RFA/Coop. Agr.)—Dr. Shannon K. Hughes

Dr. Shannon K. Hughes, Program Director, DCB, presented a concept to establish a human tumor atlas (HTA) network. Although such initiatives as TCGA and related programs have increased understanding of cancer genetics, the mechanisms associated with the molecular, cellular, and tissue interactions that facilitate critical transitions cancer are not well understood. With these gaps in knowledge, it is challenging to predict prognosis, develop risk stratification, or precision screening treatment strategies. A comprehensive view of the tumor ecosystem will improve understanding of tumor heterogeneity and evolution and understanding of the contribution of non-tumor components (e.g., stroma, immune cells, or extracellular matrix). In addition, the identification of markers of disease progression and drug resistance and development of early intervention strategies and robust therapies also will be improved. Transformative technologies and computational approaches can now facilitate studies on the comprehensive view of cancer. The goal of this RFA is to generate pilot-scale, high-priority, human tumor atlases that facilitate basic and clinical scientific discovery regarding important transitions during tumorigenesis. The HTA Network will consist of highly integrated HTA research centers focused on generating three-dimensional tumor atlases, complementary Pre-Cancer Atlas (PCA) research centers to characterize pre-malignant lesions, and HTA coordinating centers to mediate activities between the research centers through scientific and administrative support. High-priority cancers—including breast, cervical, colorectal, and esophageal cancers—have been identified as the first targets for the pilot-scale atlases and will include tumor types that are responsive or non-responsive to immunotherapy, highly metastatic, or refractory to therapy, as well as tumors representative of cancer disparities.

This RFA would support three HTA research centers (UM1), two PCA research centers (UM1), one HTA coordinating center (U24), and one HTA tissue coordinating center.

Subcommittee Review. Dr. Tuveson expressed the Subcommittee's support for the concept and noted that there is an immense potential now to capture an integrated view of live tumors. The HTA project will be an intuitive, searchable, informative, and dynamic resource for the research community. The Subcommittee suggested adding pancreatic cancer to the list of high-priority tumors, developing human tissue models of the immune system, and using rapid autopsies as potential candidates to inform the HTA.

The first year cost is estimated at $17.875 M for five UM1 awards and two U24 awards, with a total cost of $99.875 M for 5 years.

Questions and Answers

Members voiced concern about using tissue from autopsies due to the potential for lysis of inflammatory cells in those samples. Also, the technology for autopsy studies is still being developed or may need to be developed.

Dr. Wicha suggested linking the atlas to known animal models to further characterize the disease, and Dr. Sawyers commented that the Chan Zuckerberg Initiative's Human Cell Atlas would be a resource to leverage.

Dr. Lacey suggested incorporating strategies to address scalability and engage NCI's Center for Biomedical Informatics and Information Technology (CBITT)for advice.

In response to a query from Dr. Walker on tumor responsiveness, Dr. Hughes explained that the first iteration will involve generating pilot atlases within the high-priority cancers to serve as models to inform broader-scale atlases that would be applicable to other tumor types. Dr. Jaffee noted that the BRP recommendations were to extend the efforts of TCGA and address the challenges and to expand the scope to include premalignant lesions, other cancer types, and studies involving the microenvironment. The objective of the pilot-scale atlas is to generate data sets that the community could use to generate hypotheses that move the science forward.

Members recommended that the NCI consider including measures to address diverse population representations early in the development of the Cancer Moonshot RFAs and to develop a minimum data set to ensure adequate clinical annotations of data.

Dr. Bar-Sagi commented that the investments for the HTA Network were significant and that the milestones should have adjustable metrics and measures that outline the factors involved in a decision to stop the project.

Motion. A motion to approve the OD's RFA/Coop. Agr entitled "Human Tumor Atlas Network" was approved unanimously.

Approaches to Identify and Care for Individuals with Inherited Cancer Syndromes (New RFA/Coop. Agr.)—Dr. Kathy J. Helzlsouer

Dr. Kathy J. Helzlsouer, Associate Director, Epidemiology and Genomics Research Program, DCCPS, presented a concept on approaches to identify and care for individuals with inherited cancer syndromes. Dr. Helzlsouer informed members that inherited susceptibility to cancer occurs in 10 percent of all cancers, but cancer genetic counseling and testing is underutilized. Furthermore, cancers can be associated with multiple genetic syndromes, and the complexity of genetic counseling has increased over the past 2 decades. This RFA concept aims to develop and test strategies to increase case ascertainment of hereditary cancers; develop and adopt evidence-based health care delivery models for cancer prevention and detection, cascade testing of relatives, and follow-up care; test sustainable strategies to improve implementation across diverse health care settings and populations; and identify demonstration metrics for successful and sustainable ascertainment, consultation, and interpretation. Multidisciplinary, multi-investigator applications will be required and should address at least two health care delivery settings and a spectrum of hereditary cancer syndromes, focus on a continuum of care, provide outreach to diverse communities, examine behavioral/socioeconomic impact on patients, and assess care transitions.

The RFA will support four research projects (U01) in two phases, with one to two grants funded in year 1 and the remainder in year 2.

Subcommittee Review. Dr. Ian M. Thompson, Jr., President, CHRISTUS Santa Rosa Medical Center Hospital, Texas Urology Group, expressed the Subcommittee's support for the concept and noted the opportunity to improve outcomes at the population level in an area of research not supported by traditional funding mechanisms. The Subcommittee suggested increasing the funding level to ensure adequate outreach to families located in rural settings and to include adherence as a component of the examination of behavioral aspects.

The first year cost is estimated at $4 M for four U01 awards, with a total cost of $20 M for 5 years.

Questions and Answers

In response to a query from Dr. Becich, Dr. Helzlsouer replied that the RFA is not a screening protocol, but is designed to develop the process to improve ascertainment, which would be applicable to different health care settings.

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, asked about preexisting conditions and how associated privacy issues and insurance coverage would be addressed in health care settings. Dr. Helzlsouer indicated that this RFA would be one attempt to begin to address those issues.

Motion. A motion to concur on the OD's RFA/Coop. Agr. entitled "Approaches to Identify and Care for Individuals with Inherited Cancer Syndromes" was approved unanimously.

IX. 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) (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 IRG recommendations was unanimous. During the closed session, a total of 2,859 NCI applications were reviewed requesting direct cost support of $1.012,784,139 and 2 FDA applications requesting direct cost support requesting $321,502.

WEDNESDAY, 21 JUNE 2017

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

Office of the Director

Pediatric Immunotherapy Translational Science Network (New RFA/Coop. Agr.)—Dr. Malcolm A. Smith

Dr. Malcolm A. Smith, Associate Branch Chief, Pediatrics in the Clinical Investigations Branch, Cancer Therapy Evaluation Program, DTCD, presented a concept to establish a pediatric immunotherapy

translational science network (PI-TSN), noting that the name has been changed to the Pediatric Immunotherapy Discovery and Development Network (PI-DDN) per recommendations from the BSA Subcommittee. Dr. Smith stated that low mutational burdens are generally characteristic of pediatric cancers, as are the correspondingly low rates of neoantigens resulting from somatic mutations, which is the reverse of adult cancers. Therefore, pediatric immunotherapy research is distinct from adult immunotherapy research. Although immunotherapy approaches (e.g., targeting embryonal antigens or use of chimeric antigen receptor engineered T cells) have been successful in treating childhood cancers, drug resistance develops and additional agents are needed for pediatric solid tumors. The areas of focus proposed for the PI-DDN include identification of antigenic epitopes that are unique and abundantly expressed on childhood and adolescent tumors; development of optimized, highly specific binders for novel pediatric cancer immunotherapy targets; development of candidate novel immunotherapy agents; the identification of cancer cell mechanisms of resistance; and development and application of approaches for *in vivo* preclinical testing of novel immunotherapy agents. This research will leverage other NCI pediatric immunotherapy research activities.

The RFA would support a PI-DDN consisting of three to four multi-component programs (U54) to support collaborative investigator teams addressing two or more synergistic areas of focus; three to four research projects (U01) to support discrete individual or multi-investigator projects addressing a relevant area of focus (e.g., model development); Administrative Supplements for collaborations across the Network; and NCI core services to support the Network.

Subcommittee Review. Dr. Shannon expressed the Subcommittee's support for the concept, which will address an underrepresented area of research. He noted that the Subcommittee appreciates NCI staff responses to their recommendations to change the title from translational to discovery network to best fit the pre-translational–related resource building efforts (e.g., epitope identification and testing) and a rebalancing of the multicomponent programs (U54) and the projects (U01). Additionally, the Subcommittee encourages addressing cancer health disparities by including it as a component in the PI-DDN.

Questions and Answers

In response to a query from Dr. Jaffee on interrogating existing pediatric tissue biorepositories, Dr. Smith replied that the U01 investigators would be tasked with identifying novel pediatric mechanisms of sensitivity and resistance. The concept does not include tissue banks *per se*, but the expectation is that investigators would have access to these resources through the Children's Oncology Group (COG), which is composed of 200 institutions across the country.

Dr. Bondy suggested expanding the scope to include the young adult population who also would benefit from immunotherapy treatment, and Dr. Ley suggested developing mechanisms to synergize adult and pediatric incentives in the Cancer Moonshot initiatives. Dr. Singer indicated that many of the activities and interactions of Cancer Moonshot initiatives will cross-cut and that the goal is to promote those type of interactions.

The first year cost for the NCI is estimated at $8 M for three to four U54 awards and three to four U01 awards, with a total cost of $40 M for 5 years.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Pediatric Immunotherapy Discovery and Development Network (PI-DDN)" was approved unanimously.

Moonshot Coordinating Center for Mechanisms of Cancer Drug Resistance and Sensitivity Network (New RFA/Coop. Agr.)—Dr. Austin Doyle

Dr. Austin Doyle, Medical Officer, Cancer Therapy Evaluation Program, DCTD, presented a concept to establish a Cancer Moonshot drug resistance and sensitivity Coordinating Center (U24) to support the drug resistance and sensitivity network (DRSN), a network of five U54 centers that was proposed under RFA CA-17-009. The Coordinating Center will assist the DRSN centers with coordination of network activities; statistical and computational support; data management, harmonization, and protocol development; and integration into other NCI research activities, including Cancer Moonshot initiatives and the Precision Medicine in Oncology initiative. In addition, the Coordinating Center will assist the DRSN centers in interfacing will other NCI programs (e.g., PDMR) and the broader research community. Measures of success include the ability to coordinate the DRSN activities and provide a platform that facilitates data management, sharing of resources/tools, interaction with other NCI initiatives and programs, and outreach.

Subcommittee Review. Dr. Bar-Sagi expressed the Subcommittee's support of the concept. She noted that the Coordinating Center will play a critical role serving as honest broker among the DRSN centers to ensure cross-validations of paired biopsies for drug resistance biomarker discovery. The Subcommittee expressed concern about the ability to coordinate the different preclinical models of drug resistance that will be developed/interrogated within the DRSN and whether the models would be redundant or applicable to immunotherapy clinical trials.

Questions and Answers

Dr. Lacey asked about the expertise, staff, and technologies that would be needed to assist the Coordinating Center in supporting the DRSN. Dr. Doyle stated that neither Web bench analysis nor actual experiments would be supported. Support from biostatisticians or 'omics' experts is anticipated. Dr. Doroshow stated that no specific number of employees will be on staff, but several employees contributing in varying percent efforts would be needed to support the Coordinating Center, especially as projects are prioritized and resources are assessed.

In response to a query from Dr. Walker on the original coordinating plan and databases that would be maintained, Dr. Doyle replied that the U24 Coordinating Center will replace the Drug Resistance and Sensitivity Committee originally designated in the RFA CA-17-009. The Coordinating Center will facilitate data collection from and harmonization among the DRSN centers.

The first year cost for the NCI is estimated at $0.5 M for one U24 award, with a total cost of $2.5 M for 5 years.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Moonshot Coordination Center for Mechanisms of Cancer Drug Resistance and Sensitivity Network" was approved with 20 ayes, 0 nays, and 1 abstention.

Improving Management of Symptoms Across Cancer Treatments (IMPACT) (New RFA/Coop. Agr.)—Dr. Paul Jacobsen

Dr. Paul Jacobsen, Associate Director, Healthcare Delivery Research Program, DCCPS, presented a concept on Improving Management of symPtoms Across Cancer Treatments (IMPACT). Dr. Jacobsen informed members that the major barriers to effective symptom control are that symptoms are not systematically assessed and reported, nor are they adequately managed. These barriers could partly be due to the lack of systematic efforts to translate research into practice. Randomized controlled clinical

trials have shown the benefits of integrated symptom assessment and reporting, but the implementation science approach is yet to be applied. The goals of the RFA are to establish a research network, i.e., IMPACT, that will serve as a laboratory to develop scalable, transferrable, and sustainable models for monitoring and addressing symptoms in routine practice. The IMPACT network will rigorously examine the impact on symptom control and the functioning, treatment delivery, and use of health care by using the power of the network to evaluate the effects across the care continuum and for minority and medically underserved populations. These efforts are expected to produce findings and materials for wider implementation.

This RFA would support three research centers (UM1) and one coordinating center (U24). Each research center will be charged with developing and evaluating an integrated symptom management system to address symptoms across the cancer continuum. The coordinating center will support the research centers in the early stages of the project by promoting data sharing and facilitating data integration and in the later stages by examining and analyzing cross-cutting issues and developing public datasets for use by external investigators. Successful formation of a coordinated research network is expected in years 1–2. Timely completion of major milestones, including implementation of integrated network systems across practices, are anticipated for years 2–5.

Subcommittee Review. Dr. Lacey expressed the Subcommittee's enthusiasm and support for the concept. He noted that the Subcommittee suggested refining the scope and focus to include an implementation science component, clarifying the requirements for conducting clinical trials at individual sites or centers, and developing mechanisms in the long term to implement successful outcomes in a timely manner.

Questions and Answers

Dr. Becich suggested leveraging existing patient-reported outcomes networks (e.g., the Patient-Centered Outcomes Research Institute and NIH's National Center for Advancing Translational Sciences) and existing electronic health (EHR) record tools (e.g., Fast Healthcare Interoperability Resources) to establish a standard for the research centers.

In response to a query from Dr. Basch on resources to support large networks using common EHR systems, Dr. Jacobsen replied that the RFA concept is an implementation study to support smaller proof-of-concept networks to demonstrate practices reflective of representative symptom management system designs.

Ms. Smith suggested including patient and caregiver representatives on the steering committee and to consider establishing public-private partnerships. Dr. Jacobsen indicated that the Cancer Moonshot Implementation Partnership Committee will facilitate engaging potential partners.

The first year cost for the NCI is estimated at $5.4 for three UM1 awards and $0.6 M for one U24 award, with a total cost of $30 M for 5 years.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Improving Management of SymPtoms Across Cancer Treatments (IMPACT)" was approved unanimously.

Accelerating Colorectal Cancer Screening and Follow-up Through Implementation Science (ACCSIS) (New RFA/Coop. Agr.)—Dr. David A. Chambers

Dr. David A. Chambers, Deputy Director, Implementation Science, DCCPS, presented a concept on accelerating colorectal cancer screening and follow-up through implementation science. Dr. Chambers

noted that despite the more than 30 percent decrease in colorectal cancer (CRC), i.e., mortality rates in the United States from 1980 to 2014, not all States or groups have benefited equally. The NCI, through its Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium/initiative, aims to reduce the CRC mortality rates by promoting screening in the community setting. This RFA concept will leverage PROSPR and the colorectal cancer screening process model to support three two-phased research projects (UH2/UH3) and one coordinating center (U24) to test implementation strategies that substantially improve CRC screening and follow-up rates in populations where baseline rates remain low. Each research project will include a "hotspot" catchment area/population of focus and conduct a two-phased signature trial. Researchers will use common data elements, identify within the first year what milestones will be accomplished in the UH2 phase of the award, and identify local innovations to improve uptake and quality of screening, as well as follow-up. The ACCSIS signature trial components include CRC screening and follow-up, implementation practices, and community and health care settings. The coordinating center will support the research projects to achieve UH2 milestones and accomplish UH3 phase implementation and will develop and oversee the process to consider local innovation strategies.

Subcommittee Review. Dr. Martinez expressed the Subcommittee's support for the concept. She indicated that the Subcommittee appreciates NCI staff responses to their questions about the primary populations, screening history and follow-up, and cost of clinical care for the uninsured. The Subcommittee is confident that the two-phased approach will successfully evaluate implementation strategies.

Questions and Answers

Dr. Seewaldt pointed out that certain populations' reluctance to undergo screening and the lack of resources, incentives, and availability of gastroenterologists to conduct screenings in rural areas are barriers that should be addressed. Dr. Chambers noted recent reports suggesting broadening the requirements for who could perform colonoscopies in rural areas, as well as efforts across the country to develop and implement effective screening modalities to fit the needs of the population being served. Dr. Croyle added that the DCCPS/NCI has initiated discussions with other federal agencies (e.g., CMS and CDC) and nongovernmental organizations (e.g., American Cancer Society) to address potential barriers to cancer control initiatives, including CRC screening. Dr. Paskett suggested expanding the emphasis to include underinsured populations and requirements for access to care.

Dr. Basch asked how the surveillance process was being addressed in the RFA, given the challenges to identifying potential hotspot catchment areas regarding the underinsured. Dr. Chambers indicated that the surveillance has been broadened in some catchment areas and that CDC data also may be sufficient to identify hotspots. Local partnerships would be key in all cases. Dr. Paskett added that mortality rates are one way to identify potential catchment areas, and Dr. Martinez noted that Federally Qualified Health Centers could identify potential hotspots in catchment areas.

The first year cost for the NCI is estimated at $2.4 M for three UH2/UH3 awards and $0.6 M for one U24 award, with a total cost of $15 M for 5 years.

Motion. A motion to approve the OD's RFA/Coop. Agr. entitled "Accelerating Colorectal Cancer Screening and Follow-up Through Implementation Science (ACCSIS)" was approved with 20 ayes, 0 nays, and 1 abstention.

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

NCAB *Ad Hoc* Subcommittee on Cancer Centers. Dr. Wicha, on behalf of Dr. Garber, provided a report of the Subcommittee's meeting on 19 June 2017 at which Dr. Henry Ciolino, Director, Office of Cancer Centers (OCC), presented an update report on the NCI Cancer Centers Program. He informed members that the Subcommittee discussed Cancer Center activities and funding history. Recognizing that the Cancer Center Support Grant (CCSG) funding opportunity announcement (FOA) in 2010 limited Cancer Centers in that they could only request a 10-percent increase above the prior award level. As such, the Subcommittee and Cancer Center Directors sought to address this issue, which prompted the NCI to form a Cancer Center Working Group. The Working Group deliberations and subsequent report in 2014 resulted in changes to the CCSG funding structure to establish base award by type (i.e., basic, clinical, or comprehensive), overall merit score, and portfolio size. In a rebalancing effort, the NCI in 2016 allocated $40 M to the OCC to establish a new base award to undo the inequalities in funding that had resulted from prior funding rules. This raised the awards for 21 Centers including smaller and newer Centers. Members discussed the phase-out process for underperforming Centers; Cancer Center coverage geographically and its impact on patient outcomes; the changes to the CCSG application process; the definition of catchment areas and how to address the needs of the community served; the changes in requirements for shared resources; and what the designation "Comprehensive" Cancer Center means. The Subcommittee agreed that the changes have been positive and well received by Cancer Centers. In the coming weeks, the Subcommittee chair, Dr. Garber, will solicit feedback from Center directors on the review process and the Cancer Center Program, review the responses with the Subcommittee, and forward a report to the NCI for further discussions.

Questions and Answers

Dr. Chang voiced concern that reducing the descriptive language for shared resources from 12 pages to 6 pages in the application process would affect the amount of funding allocated to Cancer Centers, especially to smaller Centers. Dr. Wicha indicated that the intent is to streamline the application process, not deemphasize shared resources. Dr. Lowy expressed appreciation to Drs. Chi Dang and Stanton L. Gerson, Director, Case Comprehensive Cancer Center, Case Western Reserve University, and the Cancer Center directors for assisting the OCC and the NCI in implementing the program changes.

Motion. A motion to accept the report of the 19 June 2017 NCAB Cancer Centers Subcommittee meeting was approved unanimously.

NCAB *Ad Hoc* Subcommittee on Population Science, Epidemiology, and Disparities. Dr. Paskett provided a report of the 19 June 2017 inaugural meeting of the *Ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities. The goal of the meeting was to review activities of NCI Divisions that are concentrating on population science, epidemiology, and disparities. The Subcommittee heard presentations on clinical trials and training from Dr. Kramer, DCP; on behavioral sciences and rural disparities from Dr. Croyle, DCCPS; on the national outreach network and the geographical management of the CHD from Dr. Sonya Springfield, CRCHD; and on metrics and description of the population science programs at NCI-designated Cancer Centers from Dr. Ciolino, OCC. At the close of the meeting, members were requested to submit ideas on areas the Subcommittee should focus its attention.

Motion. A motion to accept the report of the 19 June 2017 NCAB *Ad Hoc* Population Science, Epidemiology, and Disparities Subcommittee meeting was approved unanimously.

XII. ADJOURNMENT—DRS. CHI V. DANG 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 9th joint meeting of the BSA/NCAB was adjourned at 11:12 a.m. on Wednesday, 21 June 2017.

Date	Chi V. Dang, M.D., Chair, BSA
Date	Elizabeth M. Jaffee, M.D., Chair, NCAB
Date	Paulette S. Gray, Ph.D., Executive Secretary