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

13th JOINT MEETING
of the
BOARD OF SCIENTIFIC ADVISORS AND
NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
June 10, 2019

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

BOARD OF SCIENTIFIC ADVISORS and
NATIONAL CANCER ADVISORY BOARD JOINT MEETING
BETHESDA, MARYLAND
Summary of Meeting
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The Board of Scientific Advisors (BSA) of the National Cancer Institute (NCI) and the National Cancer Advisory Board (NCAB) convened for the 13th Joint Meeting on June 10, 2019, in Conference Room TE406, East Wing, Shady Grove Campus, NCI, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Monday, June 10, 2019, from 8:30 a.m. to 4:47 p.m. and closed to the public on Monday, June 10, 2019, from 5:00 p.m. to 6:00 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 BSA Chair, Dr. Dafna Bar-Sagi, Vice Dean for Science, Senior Vice President and Chief Scientific Officer, Professor, Department of Biochemistry and Molecular Pharmacology and Medicine, New York University (NYU) Langone Health, NYU School of Medicine, presided during the open session. Dr. Jaffee presided during the closed session. In the open session, the BSA considered new requests for applications (RFAs), Cooperative Agreements (Coop. Agr.), requests for proposals (RFPs), and program announcements with special receipt, referral, and/or review (PARs) of new and re-issue concepts presented by NCI Program staff.

BSA Members
Dr. Dafna Bar-Sagi (Chair)
Dr. Kenneth C. Anderson (absent)
Dr. Michael John Becich (absent)
Dr. Mary C. Beckerle
Dr. Melissa L. Bondy
Dr. Otis W. Brawley
Dr. Graham A. Colditz (absent)
Dr. Christopher M. Counter (absent)
Dr. Carol E. Ferrans
Dr. Keith T. Flaherty
Dr. Karen E. Knudsen
Dr. James V. Lacey
Dr. Michelle M. Le Beau
Dr. Sylvia Katina Plevritis
Ms. Diane Zipursky Quale (absent)
Dr. W. Kimryn Rathmell
Dr. Leslie L. Robison
Dr. Martine F. (Sheer) Roussel
Dr. Robert D. Schreiber (absent)
Dr. Victoria L. Seewaldt
Dr. Kevin M. Shannon
Dr. David Sidransky (absent)
Dr. Ian M. Thompson, Jr. (absent)
Dr. David A. Tuveson
Dr. Robert H. Vonderheide
Dr. Eileen P. White (absent)
Dr. Kevin P. White
Dr. Cheryl L. Willman (absent)

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 (absent)
Dr. Beth Y. Karlan (absent)
Dr. Timothy J. Ley
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Mack Roach III
Dr. Charles L. Sawyers
Dr. Margaret R. Spitz (absent)
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
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS
Dr. Richard Pazdur, FDA
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH (absent)
Dr. Richard J. Thomas, DOL (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Douglas R. Lowy, Acting Director, National Cancer Institute
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, and Interim Director, Center for Global Health
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
Mr. Peter Garrett, Director, Office of Communications and Public Liaison
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Ed Harlow, Special Advisor to the NCI Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis, and Acting Director, Cancer Therapy Evaluation Program
Dr. Tony Kerlavage, Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies, Acting Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Dr. Henry Rodriguez, Acting Associate Director, Center for Strategic Scientific Initiatives
Mr. Jeff Shilling, Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Bioinformatics and Information Technology
Ms. Donna Siegle, Executive Officer and Deputy Director for Management, Office of the Director
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
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology Transfer Programs
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Debbie Winn, Acting Director, Division of Cancer Prevention
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Carolyn Aldige, Prevent Cancer Foundation
Dr. Carol Brown, Society of Gynecologic Oncologists
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Dr. Ruth Hoffman, American Childhood Cancer Organization
Dr. Steven L. Klein, National Science Foundation
Ms. Laura Levit, American Society of Clinical Oncology
Ms. Maria Lopez, Kidney Cancer Association
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. Nancy O'Reilly, American College of Obstetricians and Gynecologists

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

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I. CALL TO ORDER AND OPENING REMARKS - DRS. ELIZABETH M. JAFFEE AND DAFNA BAR-SAGI

Dr. Elizabeth Jaffee called to order the 13th Joint Board of Scientific Advisors (BSA) and National Cancer Advisory Board (NCAB) meeting and welcomed members of the Boards, *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. Jaffee and Dafna Bar-Sagi reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to accept the minutes of the 13 February 2019 NCAB meeting was approved unanimously.

Motion. A motion to accept the minutes of the 25 March 2019 BSA meeting was approved unanimously.

Dr. Jaffee called Board members' attention to future meeting dates listed on the agenda and in the Board book. She noted that the 1-3 December 2019 meeting dates were changed to 2-3 December 2019 to alleviate the Sunday travel time after the Thanksgiving holiday.

Motion. A motion to accept the change in the December 2019 dates of the BSA and NCAB Joint meeting was approved unanimously.

II. NCI ACTING DIRECTOR'S REPORT - DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Acting Director, NCI, welcomed members of both the BSA and NCAB to the 13th joint meeting of these boards. Dr. Lowy provided an update on the advances in cancer research, NCI budget, and NCI activities.

Advancing Cancer Research. Dr. Lowy called attention to the *Annual Report to the Nation on the Status of Cancer,* a collaborative effort between the NCI, Centers for Disease Control and Prevention (CDC), American Cancer Society, and the North American Association of Central Cancer Registries—which was released on 30 May 2019. The report shows a decrease in the mortality rates of 10 of the 19 most common U.S. cancers in men and 13 of the 20 most common U.S. cancers in women. The Cancer Moonshot SM Initiative, which is in its third year of implementation, conveys NCI's commitment to improving the outcome for cancer patients. In an iterative process, the NCI has developed and approved concepts and issued funding opportunity announcements (FOAs) covering each of the 10 NCAB Blue Ribbon Panel recommendations for fiscal years (FYs) 2017 to 2019. Many FOAs are proposed for FY 2020. Board members are welcome to contact Ms. Christine Siemon, Division of Cancer Biology, for access to the interactive map of the NCI Cancer Moonshot SM landscape and activities.

NCI Budget and Appropriations. Dr. Lowy reminded the Board members that the Cancer Moonshot SM funding was authorized by the 21st Century Cures Act of 2016. The appropriation of $400 million (M) for FY 2019 will be the highest of the $1.8 billion (B), 7-year funding period for the program. Beginning in FY 2020, the annual allotments will decrease by $200 M per year until the funding period ends in 2023. The NCI regular appropriations have steadily increased since FY 2015, which Dr. Lowy credits primarily to the generosity, continued commitment, and bipartisan support of Congress. The House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies (L-HHS) approved its FY 2020 spending bill markup in May 2019 and includes a $2 B increase to the NIH and $310 M increase to the NCI, which is a 5 percent increase above the FY 2019 enacted budget, and the Senate Appropriations L-HHS Subcommittee spending bill is expected in early June

2019. In addition to the annual Cancer Moonshot SM allotments, the President's proposed FY 2020 budget, which was released on 18 March 2019, also includes a $50 M annual appropriation for the new Childhood Cancer Data Initiative (CCDI) that was announced during the 12 February 2019 State of the Union Address. The total proposed childhood cancer research investment is $500 M to be allotted over 10 years. The FY 2020 House Appropriations L-HHS Subcommittee markup spending bill also includes this appropriation. Dr. Lowy explained that Ms. M. K. Holohan, Director, Office of Government and Congressional Relations, will provide a detailed report on the NIH/NCI budget process later in the meeting.

New and Ongoing Activities. Dr. Lowy remarked that the Frederick National Laboratory for Cancer Research (FNLCR) is continuing to provide advanced technology support to the extramural community. The National Cryo-Electron Microscopy Facility (NCEF), which launched in 2017, is an example of one such effort. Since its inception, the NCEF has supported extramural investigators in solving more than 200 crystal structures at a performance rate of two imaging sessions per week. Notably, the data collected in the NCEF have resulted in solving high-resolution structures impacting cancer research, including the disruptor of telomeric silencing 1-like (DOT1L) methytransferase-histone 2B (H2B)-ubiquitinated nucleosome complex, which is implicated in leukemias, and the serotonin receptor, which is being used in the development of anti-emetics for chemotherapy patients. The NCI is planning to increase the NCEF's resources to support data analysis for investigators who currently do not have these services at their respective institutions.

Dr. Lowy informed the Board members that the NCI established two new working groups, the internal Screening and Early Detection Working Group, chaired by Dr. Debbie Winn, Acting Director, Division of Cancer Prevention (DCP), and the BSA a*d hoc* Working Group on Prevention, co-chaired by Board members Drs. Graham Colditz and Judy Garber. The Screening and Early Detection Working Group has a mission to identify opportunities in screening and early detection that NCI could support if the necessary resources were available. The BSA *ad hoc* Working Group on Prevention will focus on identifying gaps in cancer prevention, which can be formulated into recommendations for the NCI.

Dr. Lowy called attention to the NCI resource, the Cancer Information Service (CIS), which has been operational for 45 years. The CIS is a free service that provides unbiased information about cancer to the public and is currently contracted with the Fred Hutchinson Cancer Research Center. The contract will be re-competed in the near future, and interested parties can apply. The NCI Office of Acquisitions will receive any questions about the re-competition.

Four Areas of Added Emphasis. Dr. Lowy outlined four areas of added emphasis for the NCI and highlighted current efforts.

Childhood Cancers. Interest in pediatric cancer research has increased significantly across the NIH and the NCI from FY 2014 to FY 2018. The number of grants the NIH awarded to support pediatric cancer research increased from approximately 500 to 800 during this period. Although many NIH Institutes and Centers (ICs) are conducting this research and are receiving awards, 80 percent of the total NIH-awarded childhood cancer grants were attributed to the NCI, with a parallel increase in the training of the next generation of pediatric cancer researchers. One major effort that is conveying NCI's commitment to improving the outlook in childhood cancers is the NCI Children's Oncology Group (COG) - led Pediatric Molecular Analysis for Therapy Choice (MATCH) trial. The trial reached accrual more rapidly than had been anticipated, and more than 400 patients had been screened by the end of 2018. Twenty-four percent of patients were eligible to receive a targeted therapy treatment across a wide range of cancers. Ten percent of patients who had tumors sequenced already have received a target therapy treatment in the trial. The NCI-COG Pediatric MATCH trial has created a collaborative framework for efficient collection, processing, and sequencing of refractory pediatric cancers. A trial interim analysis was presented at the 2019 American Society of Clinical Oncology annual meeting. In addition to the 2017 Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act appropriation, the

President's FY 2020 budget proposal includes a $50 M appropriation to support the Childhood Cancer Data Initiative (CCDI) announced during the State of the Union Address. The White House has convened several stakeholder events, which were organized by Vice President Michael R. Pence. Dr. Norman Sharpless and Dr. Lowy attended an event where the Vice President expressed to the attendees, including 15 pediatric cancer patients currently undergoing treatment and their families, the Administration's commitment to advancing childhood cancer research. Dr. Lowy informed members that the CCDI appropriations will ultimately maximize opportunities to improve treatments and outcomes for children with cancer. It is anticipated that this federated system of addressing childhood cancer data will provide insight into the relapse and refractory states of the disease. The initial efforts will focus on building interactive databases involving cooperation from disparate groups to facilitate multisource data sharing in a connected data infrastructure. The NCI expects to identify opportunities to align and integrate multiple data sources to improve data utilization for patients, clinicians, and researchers. The NCI is hosting a CCDI Symposium on 29-31 July 2019, in Washington, D.C., as a scientific planning session. Further details can be accessed from the NCI website.

Investigator-Initiated Research. Dr. Lowy remarked on the importance of basic science and investigator-initiated research to cancer breakthroughs, both of which are reflective in outcomes for patients. Although the advances in melanoma and immunotherapy have benefited many patients with metastatic disease, the prognosis for patients with glioblastomas is not as positive, signifying the need for more research. A Bentley University narrative review study of newly approved drugs from 2010 to 2016 by its Center for Integration of Science and Industry was published in the March 2018 edition of the *Proceedings of the National Academy of Sciences.* The findings were that NIH funding contributed to all 210 Food and Drug Administration (FDA) approved new drugs. Additionally, it was noted that basic research was involved in identifying the biological targets in preclinical studies, which could be translated into an intervention.

Health Disparities. Dr. Lowy informed Board members that the disparity in U.S. cancer mortality rates between non-Hispanic Whites, Hispanic Whites, non-Hispanic Blacks, and Asian/Pacific Islanders are narrow and are continuing to decrease. Trends for the American Indian/Alaska Native populations have been less stable partly due to the small sample size. The observation is that these populations have not benefitted from advances in cancer research and dissemination as much as the other groups. Since 1999, the disparity between the heart disease and cancer mortality rates in non-metropolitan (rural) areas compared to metropolitan (urban) areas has continued to widen. To address this issue and prevent further disparity, in FY 2016, the NCI established the Rural Cancer Control Research Initiative. In FY 2018, 21 NCI-Designated Cancer Centers received administrative supplements to focus on rural populations; whereas in FY 2019, requests for applications (RFAs) were issued to address rural cancer control.

Therapeutic Resistance. Dr. Lowy noted that therapeutic resistance, both intrinsic and acquired, are major causes of cancer-related deaths. The NCI established the Drug Resistance and Sensitivity Network (DRSN), a Cancer Moonshot [SM] effort, with a threefold mission to: 1) conduct preclinical research on innovative strategies to better understand and combat mechanisms of tumor resistance and exploit tumor sensitivities to anti-cancer therapies; 2) serve as a critical component to the Cancer Therapy Evaluation Program (CTEP) clinical drug development program; and, 3) provide novel agents and aiding novel combinations or therapeutic strategies in clinical settings. The DRSN is a collaborative agreement (U54) and consists of a steering committee and five consortia, each focusing on a different type of cancer. Integral to the U54 network are the administrative supplements, which support collaboration with the DRSN of investigators external to the Network.

Leadership Appointments and Vacancies. Dr. Lowy announced that Dr. Jonas Almeida is now Chief Data Scientist in the Division of Cancer Epidemiology and Genetics (DCEG); Dr. Sara Hook has been named Associate Director at NCI-Frederick; Dr. Tony Kerlavage is the new Director of the Center for Biomedical Informatics and Information Technology (CBIIT); Mr. Weston Ricks is now NCI Budget Director; and Mr. Jeff Schilling is the new NCI Chief Information Officer. He noted NCI's ongoing

recruitment efforts for directors for the Center for Global Health (CGH), Cancer Therapy Evaluation Program (CTEP), and DCP. He expressed appreciation to Drs. Robert Croyle, Acting Director, CGH, Debbie Winn, Acting Director, DCP, and Toby Hecht, Acting Director, CTEP, for stepping in to fill these roles.

In closing, Dr. Lowy reflected on the lives and careers of two leaders in the clinical and cancer research communities. He expressed NCI's condolences in the passing of Dr. LaSalle D. Leffall, Jr., who was the former Chief of Surgery at Howard University and former president of the American Association for Cancer Research (AACR), and Dr. Henry T. Lynch, the father of human genetics and the first to discover a hereditary link in cancer (i.e., Lynch syndrome).

Questions and Answers

Dr. Dafna Bar-Sagi, BSA Chair, asked about the process for receiving projects at the FNLCR and the turnaround time to completion and the timeline for funding and completing projects after the appropriations for the CCDI have been allotted. Dr. Lowy replied that the turnaround time to the FNLCR has been approximately 1 month and that the NCI had not needed to prioritize these projects in the past. With respect to the CCDI, exactly when the appropriations to expand childhood cancer research reaches the NCI will depend on Congress. The President's FY 2020 budget proposal took the first step by proposing the $50 M annual allotments, and the House Appropriations L-HHS Subcommittee followed suit in its markup spending bill.

Dr. Kevin M. Shannon, American Cancer Society Research Professor, Auerback Distinguished Professor of Molecular Oncology, Professor, Department of Pediatrics, School of Medicine, University of California, San Francisco, observed that the NIH/NCI requires including sex as a biological variable in all research proposals and now is incorporating efforts to address race/ethnicity and wondered whether other socioeconomic disparities will rise to the level of a requirement. Dr. Lowy speculated that lifestyle differences could be contributing factors to the urban versus rural cancer disparities; he was not aware of any genetic differences that would be causative. Dr. Peter C. Adamson, Chair, COG, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia, agreed that there is no genetic basis for rural/urban cancer disparities.

In response to a query by Dr. Adamson on when pediatric tumors would have a therapeutic resistance program similar to that being implemented for adult tumors, Dr. Lowy explained that immunotherapies and fusion oncoproteins are the current two main areas of Cancer Moonshot℠ focus in pediatric cancer. Programs addressing pediatric tumors and resistance are yet to be determined.

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology Research, Professor of Surgery, Professor of Pathology, Department of Surgery and Pathology, Duke University Medical Center, lauded the CCDI effort and asked about the potential for developing a biorepository to address the rarity in some types of pediatric cancers, which is limiting to research. Dr. Lowy called attention to the Childhood Cancer Survivorship, Treatment, Access and Research (STAR) Act and its requirements for pediatric biospecimens, which the NCI is actively working to implement. On 13 May 2019, the NCI convened the Enhancing Biobanking for Childhood Cancers meeting to discuss this topic and received recommendations to take a proactive approach to provide clinically and molecularly annotated pediatric biospecimens and to broadly promote data sharing of these specimens. The NCI is exploring the possibility of partnering with other countries, and discussions with the French National Cancer Institute and Cancer Research, United Kingdom, are in progress. Increasing enrollment in pediatric cancer clinical trials will remain a continued focus for the NCI.

III. LEGISLATIVE REPORT - MS. M. K. HOLOHAN

Ms. Holohan reported on the budget and appropriations, Congressional and committee changes, and other legislation of interest. She explained that the President's budget request is based on the Budget Control Act of 2011 and that for FY 2020, cuts have been proposed for all agencies, with the exception of the Small Business Administration and the U.S. Departments of Commerce, Defense, Homeland Security, and Veterans Affairs. The President's FY 2020 budget proposal includes a 12 percent decrease in funding for the NIH, a 14.6 percent decrease for the NCI, and a $50 M appropriation for the CCDI.

The Board members were reminded that the NIH/NCI budget process for the regular appropriations began with the release of the White House Office of Management and Budget funding requests on 11 March 2019, and the subsequent President's budget proposal released on 18 March 2019. Congress considers the budget request and passes a combined resolution, which they have not done for the FY 2020 budget. Although not a mandatory step in the process, the approved budget resolution provides a framework for drafting the 12 appropriations bills and is useful to appropriators and Congressional leaders. The next step in the Congressional budget process is drafting spending bills by the House and Senate Appropriations L-HHS Subcommittees. Continuing the trend started in FY 2019, Congressional appropriators are planning to package the FY 2020 Defense and FY 2020 L-HHS spending bills, which they anticipate will facilitate the passing of the bill by Congress and signed into law prior to the beginning of the FY 2020. Reiterating that the President's budget begins the budget process, Ms. Holohan noted that the Constitution entrusts Congress with the authority to set federal budgets.

Ms. Holohan said that Dr. Lowy testified at the L-HHS Appropriations Subcommittees budget hearings, the House on 2 April 2019, and the Senate on 11 April 2019. Echoing Dr. Lowy, Ms. Holohan reported on the House L-HHS Appropriations Subcommittee spending bill and proposed appropriations for the NIH and NCI. Ms. Holohan further elaborated that the Senate L-HHS Appropriations Subcommittee markup spending bill is being finalized and is expected to be released soon. Despite this progress, the spending bills will not manifest until a budget deal is approved. The debt ceiling was reinstated on 2 March 2019, and the budget caps (defense and non-defense) will return in October 2019. Without Congressional action to raise discretionary spending caps, sequestration would cut more than $50 B from non-defense discretionary spending in FY 2020. FY 2019 ends on 30 September 2019, and the next steps in Congress will be continued negotiation on budget caps or a vote to increase the debt ceiling, introduction of Senate L-HHS appropriations bill, reconciliation of the House and Senate appropriations bills, or a potential omnibus or minibus. In terms of NCI Congressional visits, on 17 May 2019, Dr. Lowy visited with Kansas Senator Jerry Moran (R) and toured the University of Kansas Cancer Center, which is an NCI-Designated Cancer Center.

Ms. Holohan noted other legislation of interest to the NCI and related activities. The STAR Act was signed into law in June 2018 and includes provisions encouraging action from the NIH/NCI to focus on childhood, adolescent, and young adult cancer survivorship research, biospecimen collection, and biobanking resources. The NCI has begun implementation activities for the STAR legislation. An RFA, Improving Outcomes for Pediatric, Adolescent, and Young Adult Cancer Survivors, was released on 11 January 2019. The first applications are being reviewed, and the second receipt deadline will be 3 January 2020. A summary of the 13 May 2019, Enhancing Biobanking for Childhood Cancers meeting, mentioned earlier by Dr. Lowy, is in development. In an ongoing related effort, the NCI hosted the fifth childhood cancer Congressional staff visit to the NIH main campus on 29 May 2019.

Ms. Holohan called attention to upcoming Congressional briefings and events that NCI staff will attend and support, including the 12 June 2019, AACR Congressional briefing on strengthening prevention of e-cigarette use in youth; the 27 June 2019, AACR, Moffitt Cancer Center, and Biden Cancer Initiative briefing on human papillomavirus (HPV)-related cancers; and the 11 June 2019, Small Business Technology Council Washington Meeting and Champion of Small Business Technology

Commercialization Awards ceremony, honoring the NCI Small Business Innovation Research/Small Business Technology Transfer Program.

IV. RESEARCH PROJECT GRANT (RPG) POOL - DR. DOUGLAS R. LOWY

Dr. Lowy presented a report on the NCI RPG Pool, prompted by the increase in the number of grant applications that outpaced the growth of the RPG Pool funding and resulted in reduced funding success rates and paylines for NCI extramural investigators. He noted that the report had been the topic of the 9 June 2019, NCAB Planning and Budget Subcommittee meeting and that those discussions were insightful. Dr. Lowy detailed NCI's areas of emphasis and strong support of the RPG Pool and the unintended consequences. This report generated with assistance from the NCI Office of Budget and Finance reviews the FY 2013-2019 period. RPG Pool funding has increased since FY 2014, and the 7-year Outstanding Investigator Award (OIA) was established in FY 2014. The Early Stage Investigator awards were extended from 5 to 7 years by the Method to Extend Research Time (MERIT) award (R37) mechanism in FY 2018, and higher paylines for these investigators were preserved. Consequently, the 2-year R21 grant awards have decreased, the number of R01 applications have increased by nearly 50 percent, and the paylines and funding success rates for the R01s have decreased. The NCI increased allocations annually to the RPG Pool to support new competing (Type 2) and noncompeting awards and, in parallel, funded the Noncompeting Continuation (Type 5) awards at 100 percent since FY 2015.

Data from the NIH Research Portfolio Online Reporting Tools (RePORT) showed that NCI competing R01 applications increased by 46 percent from FY 2013 to FY 2018, compared with a 5 percent increase for all other NIH institutes and centers (ICs). The NCI budget (i.e., regular appropriations), not including the Cancer Moonshot℠ funding, increased by 20 percent during this time period. The RPG Pool budget mirrors the NCI regular appropriations increases. Aside from the RPG Pool, the NCI budget/regular appropriations supported increases to the Cancer Center Support Grants (CCSGs) and U54 grants. The NIH IC funding success rates for R01 applications was 16.8 percent in FY 2013 and 20.2 percent in FY 2018 and, in general, increased with the NIH budget. Conversely, for the NCI, the success rates decreased from 13.7 percent in FY 2013 to 11.3 percent in FY 2018; a significant disparity compared with most other NIH ICs, despite the increased NCI budget. In FY 2018, 41 percent of the NCI overall budget supported the RPG Pool. Of the 41 percent, 55 percent funded traditional R01 grants. From FY 2009 to FY 2018, the average award costs of NCI competing R01s were lower than those of non-NCI awards, ruling out this as a factor in the decreasing paylines.

Dr. Lowy described data depicting the trends in RPG awards by funding mechanism. He noted that from FY 2013 to the present, the R01 has been the predominant grant awarded, increasing from 600 awarded annually to just under 700 awarded in FY 2018. The R21 awards have been unstable during this period, peaking at 300 awards in FY 2015 to a low of 100 awards in FY 2017, which was attributed to NCI's first-time participation in the NIH R21 Omnibus solicitation. This approach was discontinued after a 3-year trial period because the increase in the number of R21 applications as weighted against the quality of the award did not merit its continuing. Although the OIA (R35) represents a small number of grants funded, Dr. Lowy emphasized that this is a new award for the NCI and that R35 awardees typically also have an R01 grant.

In terms of trends by dollar amounts in the RPG awards, the R01 grants experienced the highest rate of increase in the number of applications received because of NCI's decision to increase the average dollar amount per R01; however, the rate still aligns with increases in the other NIH ICs. The R21 grants' lower dollar amounts, which are calculated in aggregate, are reflective of the 2-year funding cycle compared with the R01's 5-year cycle. Funding patterns for competing RPG grants showed a 15 percent success rate for unsolicited R01s in FY 2014, which had declined to 12 percent by FY 2018. The R01 RFAs' success rates increased slightly, from 13 to 14 percent. Dr. Lowy called the Board members'

attention to the resources available on the RPG funding patterns, which can be accessed from the NCI website, and additional information on the budget that can be found in the NCI *Budget Fact Book*.

Dr. Lowy explained that the NCI investments in the competing awards RPG Pool were steady at $400 M until FY 2013. Investments increased to $450 M in FY 2014, $500 M in subsequent years, amounting to $75 M annually, and totaling $300 M being added between FY 2013 and FY 2018. These investments supported what was fiscally responsible, including the dollar amount of the awards, the increased number of grants, and out-year costs. For FY 2019, the plan is to add an additional $100 M to the competing awards RPG Pool. Dr. Lowy elaborated on the projected RPG Pool amount that would be necessary for NCI commitments to continuing grants. He described three potential scenarios: 100 percent commitment to continuing awards for FYs 2019-2021, which would require $165 M in additional funds; 97 percent commitment and a 3 percent reduction over the 2-year period, warranting $108 M in additional funds; or 92 percent commitment and 8 percent reduction, requiring $18 M in additional funds, without any increases to the NCI regular appropriations.

Dr. Lowy summarized that because of the continued excitement about opportunities in cancer research, the NCI anticipates that the number of applications will continue to increase. The NCI's regular appropriations have increased for four consecutive years and, if the FY 2020 House Appropriation L-HHS Subcommittee markup spending bill is any indication, this trend is likely to continue. The NCI is committed to doing what it can to increase the paylines in FY 2020, but any long-term strategies will depend on the NIH/NCI budget.

Questions and Answers

Dr. Charles L. Sawyers, Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, Investigator, Howard Hughes Medical Institute, and Professor of Medicine, Weill Cornell Medical College, remarked that the Planning and Budget Subcommittee is proposing that the NCAB draft a letter to the NIH Director conveying its concerns on the RPG Pool funding issues. Dr. Sawyers welcomed input from Board members.

Dr. Elizabeth Jaffee, NCAB Chair, asked about ways to communicate the RPG Pool funding issues to Congress. Dr. Lowy suggested conveying that the funding consequences reflect NCI's robust basic, translational, and clinical research efforts, which have resulted in new opportunities and interest in cancer research. The current demand to fund good ideas exceeds NCI's capacity.

Dr. Electra D. 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, commented on the increased pressure on academic investigators to obtain substantial funding from the NCI as criteria for achieving promotions and to support salaries, both of which could be contributing to the increase in applications. Dr. Paskett suggested partnering with other NIH ICs to co-fund cancer research grants to help resolve the funding issues. Dr. Lowy explained that discussions on the requirements in academia and the potential for co-funding cancer grants have been ongoing in the NCI and noted that, on average, NCI grantees have 1.3 awards, a number that has remained fairly stable. Dr. Shannon suggested that the NCI consider the unintended consequences of losing potential cancer researchers to investigating other diseases in the advent of co-funding cancer-related grants with other NIH ICs.

In response to a query from Dr. Shannon on how the NCI percentage from regular appropriations to support RPGs compares to other ICs, and whether there have been any discussions on reducing the research and development contracts to build up the RPG Pool over time, Dr. Lowy responded that the NCI spends less than other ICs because of NCI's support of the various other funding mechanisms, such as the Cancer Centers Support Grants (CCSGs), and is continually adopting strategies to maximize opportunities to fund the best proposals. The NCI contracts are supporting meritorious research and are

scrutinized by program staff. Since the NCI is underfunded in all of its areas of research, exploring new resources is more feasible than reducing funding for specific areas, such as contracts.

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, encouraged the NIH/NCI to take an enterprise view of the research resources that considers the successes aside from the number of applications received by ICs.

V. NCAB *AD HOC* WORKING GROUP ON STRATEGIC APPROACHES AND OPPORTUNITIES IN POPULATION SCIENCE, EPIDEMIOLOGY, AND DISPARITIES REPORT - DRS. JULIE PALMER AND LESLIE L. ROBISON

Dr. Leslie L. Robison, Chairman, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Associate Director, St. Jude Comprehensive Cancer Center, presented the Working Group report on the NCI extramural cancer epidemiology cohort studies. He acknowledged the members and co-chair Dr. Julie Palmer, Associate Director, Slone Epidemiology Center, Karin Grunebaum Professor, Department of Medicine, Section of Hematology and Medical Oncology, Boston University of Medicine. Dr. Robison noted that the Working Group began its preparation in May 2018 and received the charge from the then NCI Director Dr. Sharpless in June 2018 to develop recommendations on how the extramurally supported cancer epidemiology cohort program could be enhanced. Discussions first focused on the areas related to the current NCI cohort portfolio. The Working Group convened a series of teleconference calls to continue discussions and invited the participation of lead investigators in existing NIH and NCI programs and initiatives, including *All of Us*; the DCEG *Connect* Cohort; the Surveillance, Epidemiology, and End Results (SEER) Program; the SEER Virtual Pooled Registry; and the NCI Cohort Evaluation Project. After discussing the goals and objectives and collecting information on cohorts, the Working Group met in person at the NCI on 24-25 January 2019, and continued deliberations in subsequent teleconference calls to begin drafting the report.

In the NCI current cohort portfolio, the Cohort Evaluation Project includes both etiology and survivorship cohorts. The Nurses' Health Study, which started in 1976, is the longest-running etiology cohort, and the most recent is the Southern Community Cohort, which began in 2001. The NCI has made a concerted effort to increase survivorship cohorts in recent years; the longest-running of these is the Childhood Cancer Survivor Study, started in 1993, and the most recent is the Bone Marrow Transplant Survivor Study, which began in 2019. Most individuals in both kinds of cohorts self-identify as Caucasian and Hispanic individuals also comprise a small fraction of both cohort types. Dr. Robison emphasized that from the Working Group's perspective, cohorts have clear advantages in some situations and can represent the most scientifically rigorous approach. Cohorts are a long-term investment, and the most useful results are derived from long-term follow-up.

The Working Group identified five key issues, which were addressed in a question format. Dr. Robison described the issues/questions and noted that the Working Group developed 38 recommendations, which are detailed in the report. He summarized the Working Group recommendations and opportunities for enhancement in each of the following five key issue categories:

***The role of cohort studies in etiologic and survivorship research in human populations*.** The recommendations are to: 1) invest in infrastructure for cohorts to address critical scientific gaps, anticipate the scientific questions of the future, and consider societal issues that are deemed to be of high importance with high impact; 2) support new and existing focused cohort studies to address the specific cancer etiology and survivorship questions and coordinate existing and planned cohorts to ensure that they are accessible resources for the broader extramural community; and 3) support the establishment or expansion of the national infrastructure for ascertainment and cancer cases follow-up.

Utility of cohorts for addressing cancer health disparities. The recommendations are to support the establishment of additional cohorts to fill existing and future gaps in the NCI cohort portfolio and additional biospecimen collection in existing cohorts that have an appreciable number of participants from a single underrepresented group.

Study design considerations for extramural cancer epidemiology risk and survivor cohorts. The recommendations are to: 1) identify opportunities for embedding cohorts in intervention trials for primary prevention, screening, and treatment; 2) incorporate serial data and biospecimen collection over time when scientifically justified; and 3) support and facilitate methodological research to identify effective approaches for longitudinal specimen and data collection.

Data sharing and collaboration. The recommendations are to: 1) ensure that guidelines or mandates for sharing cohort data consider the time investment of and academic implications for investigators who establish and maintain the cohort; and 2) promote broad data-sharing consent in new cohorts in the initial enrollments.

Funding models for cohorts. The recommendations are to: 1) continue using a Cohort Infrastructure Program Announcement for funding the necessary infrastructure; 2) explore funding investigator-initiated hypothesis-driven research based on cohorts through R grants, program project (P01s), or related mechanisms; 3) accept applications for new cohorts only in response to periodic calls for applications, rather than allowing broad submissions; 4) establish a special study section for review of new cohort applications, separate from cohort continuation reviews; and 5) develop criteria for when to suspend funding active cohort follow-up and the use of a peer review system, which considers cohort productivity and future findings.

Questions and Answers

Dr. Carol E. Ferrans, Professor and Associate Dean for Research, Director, University of Illinois Chicago (UIC) Center of Excellence in Eliminating Health Disparities, Department of Biobehavioral Health Sciences, College of Nursing, UIC, recommended a more focused effort to develop new cohorts with more individuals from underrepresented populations since a greater percentage of the population will identify with these racial and ethnic backgrounds over the future life of the cohorts. Dr. Robison agreed, noting that the report highlighted some groups most important to consider for the future. He emphasized that future cohorts should include specific groups, as appropriate, to address scientific questions in the broad population, including both majority and underrepresented groups. Underserved populations from various socioeconomic and geographic backgrounds also should be considered.

Dr. Otis W. Brawley, Chief Medical and Scientific Officer, American Cancer Society, Professor, Department of Hematology and Oncology, Professor, Department of Medicine, School of Medicine, Professor, Department of Epidemiology, Rollins School of Public Health, Emory University, informed Board members that race is not a biological factor and wondered whether existing cohort data could be generalized to the broad population. Dr. Robison explained that because risk levels and profiles can be different between populations, the sample size must be adequate to reach the appropriate statistical power. Dr. Palmer added that although cohorts with mostly white participants have provided much information, certain questions require specific populations to answer effectively. She also noted that self-reported race can lead to many differences within a population, including among socioeconomic and educational levels.

In response to a query from Dr. Shannon on exploring opportunities to partner with other NIH ICs to evaluate other cohorts (e.g., cardiovascular and/or neurocognitive effects), which could provide insight on the different health outcomes for cancer survivors, Dr. Robison explained that many discussions have been conducted and that the NCI has reached out to other ICs to discuss funding. All studies to date have been supported by the NCI. In such cases, the investigators are able to work with other ICs on R01s that utilize those cohorts.

Dr. Victoria L. Seewaldt, Ruth Zeigler Professor, Chair, Department of Population Sciences, Beckman Research Institute, City of Hope, suggested conducting genetic admixture tests to identify drug transporters or risk elements from populations other than those with which a participant self-identifies. Dr. Robison acknowledged this possibility and noted that cohorts must continue to rely on self-reporting. He added that because of the way race and ethnicity data have been collected in cohorts that have been operating for many years, understanding the numbers of participants from a given population is not always possible.

Motion. A motion to accept the final report of the NCAB *ad hoc* Working Group on Strategic Approaches and Opportunities in Population Science, Epidemiology, and Disparities was approved unanimously.

VI. RECOGNITION OF RETIRING BSA AND NCAB MEMBERS - DR. DOUGLAS R. LOWY

On behalf of the NCI, Dr. Lowy recognized the contributions made by members of the BSA whose terms of office have expired. He expressed appreciation for their service and dedication over the course of their terms. The following BSA members are retiring: Ms. Diane Zipursky Quale, J.D., Co-Founder and President, Bladder Cancer Advocacy Network; and Dr. Kevin P. White, President, Tempus Labs, James and Karen Frank Family Professor, Department of Human Genetics, Professor, Department of Ecology and Evolution, Director, Institute for Genomics and Systems Biology, Knapp Center for Biomedical Discovery, The University of Chicago.

VII. NCAB *AD HOC* WORKING GROUP ON DATA SCEINCE REPORT - DRS. CHARLES L. SAWYERS AND MIA A. LEVY

Dr. Sawyers and co-chair Dr. Mia A. Levy, Director, Rush University Cancer Center, presented the Working Group final report and acknowledged the Working Group members. In its interim report approved at the 14 August 2018 NCAB meeting, the Working Group described data science opportunities for the NCI and introduced four initial priority recommendations that the NCI could rapidly address. Subsequently, broader discussions on data science efforts continued, and after deliberations, the Working Group discussion resulted in the following recommendations, which Drs. Sawyers and Levy summarized.

Data Science Training and Workforce Development. Define additional areas of support for data science training and workforce development and expand the initial training recommendation beyond graduate students by outlining a full workforce development plan across the continuum of training. The specific recommendations are to: 1) develop a catalog of all data science training opportunities; 2) convene a workshop to agree upon the data science curriculum relevant to cancer biology and research; and 3) develop more training opportunities for biologists in various stages of their career, including later stages. Dr. Sawyers noted the recommendation to engage younger investigators earlier, including during high school and undergraduate training, in data science. They also recommend expanding training to patient advocates who serve on review panels.

Machine Learning. Establish machine-learning infrastructure for cancer research. Along with artificial intelligence, machine learning has transformed such fields as engineering and industrial science; however, opportunities in cancer research remain underutilized. Although some uses of machine learning have been easy to implement with existing data sets, Dr. Sawyers suggested that many other possibilities will be implemented only if the NCI catalyzes connections between machine-learning experts and cancer biologists. The recommendations are to: 1) develop targeted machine-learning methodology for cancer research; 2) compile large, diverse data sets for training and machine-learning algorithms; and 3) develop new funding opportunities for machine-learning research to attract a broad machine-learning community to cancer research.

Real-World Data (RWD). Facilitate the appropriate use of RWD. Dr. Levy stated the FDA's recent approval of a new indication for an existing drug based on RWD and noted that the scale at which data are collected and assessed will need to change regarding discovery and new solutions. Dr. Levy articulated the RWD recommendations to: 1) convene stakeholders around an RWD metadata model to describe the completeness of data quality; 2) create an RWD framework and criteria for evaluating and populating key concepts for electronic health records and other RWD sources; and 3) demonstrate the utility of RWD in a series of Learning Healthcare Systems reference implications. The Working Group advocates for new statistical models for understanding bias implicit in data; a new assessment of best practices for selecting and generalizability; and new research on exposures and outcomes for patients and what the key confounders may be. Dr. Levy suggested that any data framework should be created within the context of real use cases. For example, real-world data sets could be used to design clinical trial eligibility criteria, and a standard-of-care trial arm could be replaced with a retrospective cohort based on health record data. The Working Group endorsed realigning the incentives for physicians to enter information in the electronic health record, which will require investment in studying new experimental models.

Enable the Cultural Shift Toward Data Sharing. To align with the NCI initiatives in population health, Dr. Levy detailed the specific recommendations to: 1) develop best practices and common language for broad consent; 2) streamline data-sharing policies and requirements, including access to data; 3) provide appropriate funding and resources to support data sharing; 4) develop training for data management processes and policies; and, 5) create systems to attribute and credit investigators for sharing their data.

Questions and Answers

Dr. Max S. Wicha, Madeline and Sidney Forbes Professor of Oncology, Director, Forbes Institute for Cancer Discovery, Founding Director Emeritus, University of Michigan Rogel Cancer Center, Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan, asked how industry-sponsored trials fit the data-sharing architecture in terms of investigator-initiated research and the Specialized Programs of Research Excellence (SPOREs) and wondered about bridging the gap on proprietary data sharing from industry. Dr. Sawyers explained that although he thinks the conversation is moving in the right direction regarding data sharing in the industry setting, the NCI is not likely the one to influence industry to share proprietary data; the NCI could serve as an example by sharing all other available data as appropriate.

In response to a query from Dr. Bar-Sagi on the potential relationship with private-sector entities, such as Google and Facebook, Dr. Levy commented that such entities have expressed interest in clinical data and have participated in many data science challenges because of the opportunity to work with a data set that has been well curated and validated.

Dr. Kevin White encouraged the NCI to create a program that incentivizes ICs to share data with each other. He added that acquiring follow-up response data to create ongoing longitudinal records, as well as creating incentives for physicians to enter data as they treat a patient over time, is a significant challenge that requires more attention and insights from the committee.

Dr. Ali-Osman pointed out the challenges of integrity and security for RWD. Dr. Levy explained that the Working Group final report contains recommendations that include ways to address transparency and accuracy around data quality. She noted that security is a different issue that needs additional work.

Dr. Melissa L. Bondy, Professor and Associate Director, Department of Medicine, Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, commented on the importance of ensuring that consent includes broad data-sharing over time.

Dr. James V. Lacey, Jr., Director and Professor, Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute, City of Hope, sought clarity on whether the report looks at RWD as an extension from clinical trials or more broadly, as all observational research and participant data. Dr. Levy clarified that the broadest sense includes electronic health record data, data from patient-reported outcomes, data from wearable health technology, billing data, data collected from basic or clinical research, and data from registries. Dr. Sawyers added that the most compelling near-term use case would be for patients not on clinical trials but being treated with the synthetic control, which has led to the extensions of FDA labeling. He also noted that although data security and validation have many challenges, success has been achieved in many small ways, so he encouraged considering these challenges achievable.

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, suggested that the biggest challenge is the ability to translate data into a form usable by the lay public without creating misinformation that could cause harm. Dr. Sawyers noted that increased collaboration between data scientists and cancer biologists will help to generate new ideas and will ensure that this type of concern is taken into consideration.

Motion. A motion to accept the final report of the NCAB *ad hoc* Data Science Working Group was approved unanimously.

VIII. RFA/COOP. AGR./RFP AND PAR CONCEPTS—NEW AND RE-ISSUE—NCI STAFF

Division of Cancer Treatment and Diagnosis (DCTD)

Pediatric Brain Tumor Consortium (Re-Issue RFA/Coop. Agr./Limited Competition) - Subcommittee and Dr. Malcolm A. Smith

Dr. Malcolm A. Smith, Program Director, Clinical Investigations Branch, DCTD, presented the re-issue concept to continue the research activities of the Pediatric Brain Tumor Consortium (PBTC), which the NCI has supported through successive FOAs since 1999. Dr. Smith informed members that the PBTC is the primary source of NCI-sponsored clinical trials for children with relapsed or refractory brain tumors. The PBTC is composed of 12 institutions with operations and data management housed at St. Jude Children's Research Hospital (SJCRH). The PBTC has served a key role in evaluating agents with immunological mechanisms of action for pediatric brain tumor populations and has brought novel agents into clinical testing. Most of PBTC's work involves performing initial studies in children based on prior studies on adult tumors. The PBTC is conducting the first prospective safety and feasibility trial in children for Optune, a device currently approved for adults with high-grade glioblastoma. PBTC studies often include genomic characterization and pharmacokinetic analyses. Current scientific directions for the PBTC include developing novel: 1) agents based on the distinctive biology of pediatric brain tumors, 2) local therapies, and 3) immunotherapies.

Dr. Smith highlighted the PBTC accomplishments from FY 2013 to FY 2019. He noted that the PBTC has updated its clinical trials infrastructure by integrating its systems and procedures with the CTEP and has begun to verify 100 percent of its source data through central monitoring. Operations staff rigorously review site performance and allow new institutions to join the Consortium. The PBTC worked to enable SJCRH to serve as an Investigational New Drug sponsor for trials, which facilitates the testing of a wider range of pharmaceutical agents.

The RFA will support PBTC operational enhancements, including increasing capacity for clinical trials, increasing the number of member institutions, and enhancing the PBTC's ability to collaborate with the Children's Oncology Group (COG) Central Nervous System Tumor Committee. Adding institutions

will increase scientific input to the PBTC and increase accrual support for Phase I and II trials as well as pilot studies.

Subcommittee Review. Dr. Shannon expressed the Subcommittee's enthusiasm in support of the re-issue concept. Dr. Shannon remarked that research is needed to seek higher-quality and less-toxic treatments for pediatric brain tumors. The PBTC's work differs from the COG's by bringing together investigators from neurosurgery, neuroradiology, neuropathology, and radiation oncology. The PBTC's site performance procedures align with prior Subcommittee reviews. Dr. Michelle M. Le Beau, Director, The University of Chicago Medicine Comprehensive Cancer Center, expressed that the PBTC represents a distinct and critical role within the NCI portfolio for pediatric brain tumor research for its ability to conduct timely evaluation of innovative therapeutic approaches in cooperation with other research groups.

The first-year cost for the one-time issuance is estimated at $12 M for four UM1 awards, with a total cost of $60 M for five years.

Questions and Answers

In response to queries from Dr. Wicha on the potential for using the proposed CCDI appropriations as an opportunity to explore new directions in pediatric research and funding from private foundations, Dr. Smith responded that the focus is on a new data initiative. The PBTC, including its pediatric brain tumor researchers, will be represented at the NCI CCDI Symposium on 29-31 July 2019 to discuss how the data initiative might progress. Dr. Smith explained that the PBTC has patient advocates on its steering committee who are involved in fundraising and noted that the Consortium's infrastructure provides a potential avenue for organizations to make meaningful financial contributions.

Motion. A motion to concur on the Division of Cancer Treatment and Diagnosis' re-issue Request for Applications/Cooperative Agreement/Limited Competition entitled "Pediatric Brain Tumor Consortium" was approved with 14 ayes, zero nays, and 2 abstentions.

Division of Cancer Treatment and Diagnosis

Clinical Trials Information Management and Support (CTIMS) Contract (new RFP)— Ms. Andrea Denicoff

Ms. Andrea Denicoff, Head, Clinical Trials Operations, National Clinical Trials Network (NCTN), Clinical Investigations Branch, Cancer Therapy Evaluation Program (CTEP), DCTD, presented the Clinical Trials Information Management & Support (CTIMS) contract RFP concept. The CTIMS, which has been in existence for 20 years is being reviewed by the BSA for the first time due to a new categorization of research and support contracts. Sixty percent of the CTIMS contract supports NCI's DCTD, and 40 percent supports the Coordinating Center for Clinical Trials (CCCT) by providing project management, organizational infrastructure coordination, information management, and scientific evaluation. The contract's purposes are the facilitation of efficient and effective development, review, and completion of NCI-supported clinical trials and related scientific projects.

The CTIMS contract's major areas of focus are the DCTD's Experimental Therapeutics Clinical Trials Network (ETCTN), which supports drug development arising from NCI's Experimental Therapeutics Program (NExT), and NCTN, which coordinates large precision-medicine trials, including the adult and pediatric MATCH trial, as well as a new myeloid neoplasms effort. CTIMS monitors accrual for both the ETCTN and NCTN. Ms. Denicoff emphasized the key role of CTIMS project managers (PMs) in coordinating these efforts. CTIMS provides scientific program management for several Cancer Moonshot℠ efforts, including the DRSN, Cancer Immune Monitoring and Analysis Center (CIMAC) and Cancer Immunologic Data Commons (CIDC) Network, and NCI Community Oncology Research Program (NCORP) Biospecimen Procurement Protocol. Also supported are the

NCTN Core Correlative Science Committee (CCSC), the Developmental Therapeutics Clinic Data Safety and Monitoring Committee, and the Correlative Science Studies Reviews.

Ms. Denicoff highlighted the CTIMS scientific program support accomplishments, including additional PM support for new Cancer Moonshot℠ initiatives as they are approved by the BSA. In terms of information management accomplishments, the CTIMS supported the publication of data sets for 35 completed trials involving 32,725 patients for the NCTN/NCORP Data Archive, which began in February 2017. Standard Operating Procedures for the Clinical Trials Stewardship Committee were developed, and reviews were coordinated to facilitate NCI's compliance with new NIH requirements for monitoring and oversight for clinical trials.

For the CCCT, the CTIMS supports more than 12 disease-specific scientific steering committees (SSCs). Accomplishments for these SSCs include reviewing new or revised trial concepts and biomarker proposals, coordinating task forces, supporting more than 40 working groups and subgroups, and coordinating planning meetings. In 2018, CTIMS began support for the Clinical Trials and Translational Research Advisory Committee and its associated working groups.

In the next phase of the RFP, CTIMS seeks to enhance flexible and quality PM support to new and ongoing clinical trials networks, precision-medicine trials, and scientific programs, maintain and optimize information management support to facilitate harmonized data sharing, and enhance coordination of NCI steering committees. Ms. Denicoff remarked that the complexity of NCI's scientific teams has increased throughout the past decade, requiring strong contractor support. CTIMS is supporting new scientific projects and a growing number of collaborative precision-medicine trials.

Subcommittee Review. Dr. Sawyers expressed the Subcommittee's strong enthusiasm in support of the concept. Dr. Sawyers emphasized the importance of effective oversight procedures to monitor the quality of contractor support to meet NCI objectives and goals. The Subcommittee is comfortable with CTIMS' oversight procedures.

Motion. A motion to concur on the Division of Cancer Treatment and Diagnosis' new Request for Proposals entitled "Clinical Trials Information Management and Support Contract" was approved with 15 ayes, zero nays, and 1 abstention.

IX. REPORT OF THE BSA *AD HOC* WORKING GROUP ON IMMUNOLOGY OF THERAPIES & VACCINES AND RESEARCH—DR. BLOSSOM DAMANIA

Dr. Blossom Damania, Boshamer Distinguished Professor Vice Dean for Research, School of Medicine Director, Programs in Virology and Global Oncology, Lineberger Cancer Center, The University of North Carolina at Chapel Hill, presented the Working Group final report. Providing background on HIV and AIDS malignancies, Dr. Damania explained that cancer is one of the leading causes of death in persons with HIV in North America. The AIDS-defining cancers (ADC) and non-AIDS-defining cancers (NADC) combined kill more persons with HIV on antiretroviral therapy than any other cause. Furthermore, ADCs continue to remain a problem in persons with HIV globally. Although rates have declined since the initial period of the HIV epidemic, the global burden of Kaposi sarcoma (KS) and non-Hodgkin's lymphoma remain. KS-associated herpesvirus (KSHV) is the causative agent of KS, which is the most common tumor in men in areas of sub-Saharan Africa. Approximately 44,000 new cases are reported annually, and 27,000 deaths occur annually. Studies indicate that in the United States, HIV infection is associated with a higher cancer risk in the elderly, and they also show increasing incidence over time for NADCs.

The NCI BSA *ad hoc* Subcommittee on HIV and AIDS Malignancies, consisting of 19 members, met face-to-face on 21 June 2017 to discuss specific recommendations for research and malignancies in the population positive for HIV and examined several topics of AIDS-associated malignancy research in

order to define the key issues. Recognizing that knowledge gaps exist, the Subcommittee proposed establishing two working groups to discuss: 1) issues related to oncogenic virus transmission, immune responsiveness, and vaccine development and 2) research infrastructure for HIV-associated malignancies. The NCI, however, decided that it would be best to form a single working group to consider both issues. The Subcommittee report was presented at the 27 November 2017 Joint BSA/NCAB meeting; subsequently, the BSA approved establishing the BSA *ad hoc* Working Group on Immunology of Therapies & Vaccines and Research Structure. The report can be accessed from the NCI website.

The Working Group, composed of Dr. Damania as chair and nine members representing academia and industry, was charged to provide recommendations to the Subcommittee on HIV and AIDS Malignancy. Dr. Damania acknowledged the Working Group members and indicated that their charge was to prioritize the immunological aspects of developing therapeutic and preventative therapies for virus-induced malignancies seen in HIV infection and understanding the interactions between the immune system and oncogenesis in tumor development. The Working Group also was asked to prioritize understanding transmission of oncogenic viruses that cause HIV malignancies, especially KSHV, and ways that the research infrastructure for AIDS-associated malignancies could be enhanced. The Working Group which met via teleconference on 13 June 2018, and on 8 November 2018, developed and deliberated on five major topics that aligned with the Working Group charge and purpose, which was developed into a final report. Dr. Damania summarized the recommendations as follows for:

Understanding KSHV. Among oncogenic viruses, the transmission of KSHV is the most poorly understood. Recommendations: 1) organize a symposium on KSHV focused on gaps in current knowledge on KSHV transmission and host immune responses to KSHV and 2) the feasibility of and barriers to developing a KSHV vaccine should be considered.

Obtaining cancer biospecimens from individuals infected with HIV. Biospecimens are required to advance scientific research in all HIV-associated malignancies. Recommendations: 1) establish a biorepository of specimens from HIV patients who then would be followed for the development of cancer; and 2) existing clinic-based cohorts, such as the Multicenter AIDS Cohort Study (MACS)/Women's Interagency HIV Study (WIHS), Centers for AIDS Research (CFAR), Network of Integrated Clinical Systems (CNICS), and Veterans Aging Cohort Study (VACS), could be explored and leveraged, as well as the network of global centers for AIDS research (U54 sites).

Promoting individual investigator-initiated research within the HIV malignancy field. Recommendation: Create targeted funding opportunities that bolster cross-disciplinary research to stimulate new research frontiers and advance understanding of HIV malignancies.

Motion. A motion to accept the final report of the BSA *ad hoc* Working Group on Immunology of Therapies & Vaccines and Research Structure was unanimously approved.

X. RFA/Coop. Agr./RFP/ PAR Concepts—NEW AND RE-ISSUE—NCI Staff

Division of Cancer Prevention

Chronic Pancreatitis, Diabetes, and Pancreatic Cancer Consortium (Re-Issue RFA/Coop. Agr.) - Subcommittee and Dr. Jo Ann Rinaudo

Dr. Jo Ann Rinaudo, Program Director, Cancer Biomarkers Research Group, DCP, presented the request for renewal of the joint NCI, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (CPDPC) Consortium concept. The NCI-NIDDK CPDPC Consortium was funded in 2015 to gain insight into the pathophysiology of chronic pancreatitis, pancreatic insufficiency, type 3c diabetes mellitus (T3cDM), and, especially, the association between diabetes and pancreatic cancer. The NCI-supported research focuses on the diabetes-cancer

association, whereas the focus of the NIDDK-supported research is on adult and pediatric chronic pancreatitis and T3cDM. The Consortium has four major projects: three NIDDK (restate chronic pancreatitis, pediatric pancreatitis, and type 3c diabetes) and one NCI (new-onset diabetes (NOD). Ancillary studies, which are small exploratory studies, are also conducted in the Consortium.

Dr. Rinaudo explained that persons with NOD who are between the ages of 50 and 85 are at increased risk of developing pancreatic ductal adenocarcinoma (PDAC) or pancreatic cancer. The cumulative incidence rate over three years is 0.85 percent, and patients are at a six- to eightfold risk of developing cancer three years after being diagnosed with diabetes. In addition, 25 to 40 percent of patients with PDAC develop diabetes 6 to 24 months prior to a PDAC diagnosis. She informed members that the NCI is initiating a study to investigate NOD.

The NOD project will accrue a cohort of 8,000 NOD patients with the goals of estimating the probability of PDAC, establishing a biobank of clinically annotated specimens, performing validation studies of promising biomarkers, and providing a platform to develop future interventions and screening protocols. The NOD study sites, nine CPDPC and two NCORP sites, were approved and activated in the fall of 2018, and the first patients were recruited in late fall of 2018. Each site will recruit 4,000 patients in the study at estimated rates of 2 to 3 per week per site, culminating in 1,000 to 1,200 patients in the first year. Additional sites also are being considered. As of May 2019, approximately 75 patients have been recruited into the NOD study. Dr. Rinaudo noted the initial accrual challenges and lessons learned in the recruitment sites and approaches to overcome these challenges to increase study accrual. As such, efforts were focused to maximize high-volume sites (e.g., Kaiser Permanente Northern California, Geisinger, etc.), add satellite sites in high-NOD-incidence areas, develop multilingual consent forms, change the eligibility criteria to one A1c level, and establish study milestones.

The RFA reissue will support the CPDPC Consortium in meeting its goals of maintaining the infrastructure and core facilities and providing a platform for clinically relevant studies using the biospecimens and cohorts accrued during the first grant cycle. The CPDPC clinical sites will focus on completing enrollment and collecting biospecimens in the prospective cohort studies and providing follow-up to assess clinical outcomes.

Subcommittee Review. Dr. David A. Tuveson, Roy J. Zuckerberg Professor, Director of the Cancer Center, Cold Spring Harbor Laboratory, expressed the Subcommittee's support of the re-issue concept, which is addressing a critical need. Dr. Tuveson remarked that pancreatic cancer is one in which the U.S. mortality rates continue to increase despite new advances in cancer research. In patients who survive pancreatic cancer, their disease was detected early. Complicating matters is that no biomarker exists to detect pancreatic cancer. Dr. Tuveson stated that discussions in the NCI Early Detection Research Network suggest that a lack of a biomarker is perhaps the result of the lack of established biobanks of patient samples or data, especially of persons who are at high risk for developing pancreatic cancer. Although the increased blood sugar/pancreatic cancer correlation is not new information, the opportunity exists to systematically study the relationship, identify early-stage disease, and assess exocrine diabetes (i.e., T3cDM). The Subcommittee appreciates NCI staff responses to their questions about accrual, approaches to overcome recruitment challenges, and study milestones. The NCI could consider coordinating the research projects across its programs and initiatives that are focused on pancreatic cancer.

The first-year cost for the one-time issuance is estimated at $2.3 M for 10 U01 awards, with a total cost of $11.5 M for five years.

Questions and Answers

Dr. Wicha queried staff regarding the scientific hypothesis underlying the NOD project. He noted that the goal of enrolling high-risk patients is clear. However, will addressing pancreatic cancer metastasis in the

early stages and understanding the biology that relates diabetes to cancer be addressed? Dr. Rinaudo explained that basic science research is conducted within the Consortium and also is a focus in some of the ancillary studies.

Dr. Karen E. Knudsen, Hilary Koprowski Endowed Professor, Chair, Department of Cancer Biology, Director, Sidney Kimmel Cancer Center, Thomas Jefferson University, asked about the criteria for the additional sites to be included in the NOD study. Dr. Rinaudo said that any additional sites for the study will need to show evidence of successful accruals, access to the NOD patient population, and present a scientific question that they could address, if funds become available. Essentially, the additional sites will need to address the approaches to overcome challenges NCI indicated and increase study accrual. Although the focus of the RFA is on the accrual rather than scientific merit, Dr. Bar-Sagi suggested giving weight to the scientific question in the future, which might direct the types of samples collected in the study. Dr. Rinaudo clarified that the RFA is supporting a cohort study, the initial criteria will be NOD, and patient samples will be collected, but an algorithm will select/predict high-risk patients. The Consortium's ancillary studies can, in parallel, focus on a scientific question, making use of patient samples.

Motion. A motion to concur on the Division of Cancer Prevention's re-issue Request for Applications/Cooperative Agreement entitled "Chronic Pancreatitis, Diabetes, and Pancreatic Cancer Consortium" was approved with 7 ayes, 6 nays, and 3 abstentions.

Office of the Director (OD)

U.S. and Low- and Middle-Income Country (LIMC) HIV Malignancy Research Networks (new RFA/Coop. Agr.) - Dr. Geraldina Dominguez

Dr. Geraldina Dominguez, Program Director, Office of HIV and AIDS Malignancy, OD, presented a concept to establish the U.S.-LIMC HIV Malignancy Research Networks. Dr. Dominguez informed members that in 2016, the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that approximately 37 million people were living with HIV worldwide. She noted that more than two-thirds live in sub-Saharan Africa, and southern and eastern Africa. Asia and Latin America also are heavily affected areas. Among U.S. males, the most common cancer is melanoma skin cancer. Among females, breast cancer is most prevalent. In countries like Botswana, Mozambique, and Malawi, the most common cancer among males is Kaposi sarcoma (KS), an AIDS-defining cancer, and cervical and breast cancer are most common among females. In fact, cervical cancer is the most prevalent cancer in 27 countries, many of which are in sub-Saharan Africa. These countries also experience a heavy HIV burden.

Dr. Dominguez highlighted two initiatives in which the NCI and the NIH Fogarty International Center have worked towards developing research capacity in low-resource settings. Phase 1, the sub-Saharan African Collaborative HIV and Cancer Consortia, was limited to Africa. Phase 2, the Collaborative Consortia for the Study of HIV-Associated Cancers: U.S. and LIMC Partnerships expanded to include other LMICs. Phase 1 and Phase 2 formulate the Collaborative Consortia in HIV-Associated Cancers (Collaborative), share similar goals, and provide the framework for this RFA concept. Eleven consortia, 10 in sub-Saharan Africa and one in South America, comprise the Collaborative, and each consists of a partnership between a U.S. institution and an LMIC institution. Leadership is shared between U.S. and LMIC investigators, and the program structures are similar in terms of research projects, shared research, mentoring/career enhancement, and administration cores. The most common research topics are HPV, KS-associated herpesvirus, lymphoma, and liver cancer. Dr. Dominguez highlighted the accomplishments of Phase 1 and Phase 2. The Collaborative Consortia developed regional hubs for translational research in HIV-associated cancers, generated 49 publications, supported new grant submissions for young investigators, and developed a novel model for career development focusing on peer mentoring.

This RFA will expand the achievements of Phase 1 and 2 and will initiate Phase 3 with four overarching goals: accelerate scientific knowledge in HIV-associated cancers, develop research capacity in LMICs with a significant burden of HIV-associated cancers, support collaborations between U.S. investigators and LMIC investigators, and foster the development of early-career investigators from the United States and LMICs who are interested in conducting research on HIV-associated cancers. The Phase 3 RFA will expand to multi-institutional networks, multiple principal investigator applications, mechanistic studies, and support for career development for junior investigators. This concept is tentatively approved by the Office of AIDS Research (OAR) as a FY 2020 NCI initiative and aligns with the recommendations of the BSA *ad hoc* Subcommittee on HIV/AIDS Malignancy. The NCI-appropriated AIDS funds, as established by the OAR, will support this research.

Subcommittee Review. Dr. Lacey expressed the Subcommittee's enthusiasm for and support of the concept. He noted that the Subcommittee was impressed with the accomplishments of Phase 1 and 2 and the international partnerships and thinks that expanding to a Phase 3 is a worthwhile endeavor. The Subcommittee appreciates NCI staff responses to their questions on the type of research that will be supported, leveraging the success of the Phase 1 and 2 collaborative partnerships, OAR funding, and training. However, consideration should be given to indicating in the RFA that the solicitation is open to all and is not limited to those in the collaborative consortia in HIV-associated cancers. Additionally, the RFA evaluation criteria should be reconsidered.

The first-year cost for the one-time issuance is estimated at $19.7 M for six U24 awards, with a total cost of $118.4 M for six years.

Motion. A motion to concur on the Office of the Director's Request for Applications/Cooperative Agreement entitled "U.S. and Low- and Middle-Income Country (LMIC) HIV Malignancy Research Networks" was approved unanimously.

Division of Cancer Treatment and Diagnosis

Biospecimen Banks to Support NCI National Clinical Trials Network (NCTN) NCI Community Oncology Research Program (NCORP) and CTEP-Supported Early Trials/Studies (Re-Issue RFA/Coop. Agr. /Limited Competition) - Subcommittee and Dr. Irina Lubensky

Dr. Irina Lubensky, Chief, Pathology Investigation and Resources Branch, DCTD, presented the biospecimen banks to support the NCTN clinical trials re-issue concept. Dr. Lubensky informed members that the goal is to collect, process, store and distribute well-annotated NCI clinical trials biospecimens for research. The RFA currently supports five biospecimen banks, four adult banks (Alliance for Clinical Trials in Oncology (ALLIANCE); Southwest Oncology Group (SWOG); Eastern Cooperative Oncology Group–American College of Radiology and Imaging Network (ECOG-ACRIN); NRG Oncology [National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG)]; and, one pediatric bank, the Children's Oncology Group. The principal investigators are pathologists specialized in biospecimen banking, and the supported banks form a collaborative Network and engage with the NCTN trial groups and the statistical and operations centers. Specimens collected for NCTN Phase II, Phase III, and other trials on protocols are well annotated with clinical and outcome data and used by NCTN trial group investigators for integral and integrated biomarker studies/assays. All organ sites and adult and pediatric cancer specimens are collected. Any specimens remaining in excess after clinical trial requirements have been met become "legacy" specimens and are available to investigators for secondary correlative studies, following a defined NCTN biospecimen access and approval process.

Dr. Lubensky noted that between 2013 and 2017, the NCTN Banks collected 1,642,567 trial specimens and distributed 440,144 specimens to 223 NCTN investigators and 348 legacy samples to NCTN Group and non-NCTN Group investigators. There were 572 publications resulting from specimens

used for research. Aside from contributing to translational and clinical science, many specimens changed clinical practice. In addition, the NCTN banks contributed specimens to many trans-NCI initiatives, including the Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials, the Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments, and the Cancer Moonshot℠. The Network responded to prior BSA recommendations on improving access to legacy biospecimens and developed and launched the NCTN Navigator and Front Door Service, a web-based clinical specimen and data resource, on 2 April 2018. The NCTN Navigator is hosted by the Cancer Trials Support Unit/CTEP, and the goals are to consolidate biospecimen inventory, connect biospecimens and clinical data, provide biospecimen access to the research community, and track applications from receipt to publications. Investigators can explore the inventory from the NCTN Navigator website and will be guided by the centralized NCTN-Biospecimens 'Front Door' process. As of 29 May 2019, published data from 119 clinical trials had been loaded, which includes 72,363 patient cases and 852,946 specimens. While only adult cancer cases have been loaded, loading pediatric cancer cases is in progress. The NCI staff responded to the BSA reviewers' comments, which have informed changes to the program.

The RFA re-issuance will support continuing services of the five NCTN biospecimen banks and expanding the Network to include an Early Clinical Trials bank to support the ECTCN, Cancer Immunology Trials Network (CITN), and Cancer Immune Monitoring and Analysis Centers (CIMACS). Also supported will be the NCTN banks infrastructure and operations, new functions, NCORP cancer prevention trials, and new PEP-CTN biospecimen banking in the COG NCTN bank, which aligns with the implementation of the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR Act).

Subcommittee Review. Dr. Knudsen expressed the Subcommittee's enthusiasm and support of the re-issue concept. The Subcommittee recognized several strengths of the NCTN Banks in their support of the clinical trials networks and cooperative groups. Dr. Knudsen noted that the research findings resulting from the use of the biospecimens have been significant, as have the published data. The Subcommittee suggested reducing the lag time for receiving specimens, clarifying the demand metrics, and establishing mechanisms to ensure that investigative efforts are not duplicated.

The first-year cost for the one-time issuance is estimated at $2.3 M for four UM1 awards, with a total cost of $11.5 M for five years.

Questions and Answers

Dr. Martine F. Roussel, St. Jude Children's Research Endowed Chair in Molecular Oncogenesis, Full Professor, Department of Molecular Sciences, The University of Tennessee, Full Member, Department of Tumor Cell Biology, St. Jude Children's Research Hospital, asked about the rationale for increasing the RFA budget. Dr. Lubensky responded that the budget for the NCORP cancer prevention trials, $1.8 M, has already been approved and is reflected in the overall budget request. The costs of the NCTN banks infrastructure changes and new functions also warrant increasing the budget.

Dr. Kevin White suggested including only some of the data elements associated with the clinical trials, rather than all trials' curated data and wondered whether user fees would offset the budget. Dr. Lubensky explained that user fees are charged for specialized services but contribute to less than 50 percent of the NCTN banks operational expenses. The RFA subsidizes the cost of biospecimen collections.

Motion. A motion to concur on the Division of Cancer Treatment and Diagnosis' re-issue Request for Applications/Cooperative Agreement/Limited Competition entitled "Biospecimen Banks to Support NCI National Clinical Trials Network (NCTN), NCI Community Oncology Research Program (NCORP), and CTEP-Supported Early Trials/Studies" was approved unanimously.

Division of Cancer Control and Population Sciences (DCCPS)

Co-Infection and Cancer (new PAR)—Dr. Tram Kim Lam

Dr. Tram Kim Lam, Program Director, Environmental Epidemiology Branch, DCCPS, presented the PAR concept of Co-infection and Cancer, a trans-NCI initiative in collaboration with the DCCPS, DCB, DCP, CGH, and Center to Reduce Health Disparities (CRCHD). The overarching purpose is to enhance mechanistic and epidemiologic research in co-infection and cancer and to identify markers for early detection and prevention. Co-infection is defined as the occurrence of infections by two or more infectious (pathogenic or non-pathogenic) agents, either concurrently or sequentially, and includes both acute and chronic infections by viruses, bacteria, parasites, and/or other microorganisms. Co-infection with HIV is excluded from this FOA.

Dr. Lam explained that infectious agents play a role in the etiology of cancer and contribute to the global cancer burden. Approximately 15 percent of new cancer cases have been estimated to be caused by infectious agents. Several well-known cancer-causing pathogens exists. The Epstein Barr virus (EBV) was first implicated in Burkitt's lymphoma. Hepatitis B and C viruses are established risk factors for liver cancer. Human papillomavirus (HPV) is causative to many cancers, including cervical cancer. The bacterium *Helicobacter pylori* (*H. pylori*) is an established risk factor for stomach cancer. The prevalence of these pathogens varies by geographical location, mirrors the incidence of cancer, varies by race/ethnicity, and presents a higher burden in developing countries than non-developing countries. Approximately 80 percent of Americans are infected with EBV and 30 percent with *H. pylori*. The prevalence of *H. pylori* infection is higher among African Americans than among Caucasians, and similar patterns are observed in the Hispanic population.

Although most people with cancer-causing pathogens are chronic carriers, they rarely develop the associated cancer, suggesting that infection-driven cancer initiation and progression may require additional cofactors. The body of evidence emerging from the research studies suggests that the presence of another infectious agent may be the necessary cofactor for infection and related cancer initiation and progression. The etiologic role of co-infection in cancer risk is suspected but is relatively unknown. The mechanism of co-infection in carcinogenesis also is not well understood. The identification of a risk profile may lead to targeted interventions and prevention strategy. This PAR concept will investigate the involvement of both pathogenic and non-pathogenic agents in the development or progression of cancer and will address the gap in research and within the NCI research portfolio.

Subcommittee Review. Dr. Michelle M. Le Beau, Arthur and Marian Edelstein Professor of Medicine, Director, University of Chicago Medicine Comprehensive Cancer Center, The University of Chicago, expressed the Subcommittee's enthusiasm for and support of the PAR concept, which addresses an understudied area. Dr. Le Beau remarked that this concept could enhance mechanistic and epidemiologic investigations on the role of co-infection and cancer, catalyze other related research interests, and provide opportunities to collaborate internationally, which the NCI could facilitate. The Subcommittee suggested framing the message to convey that not all prior studies have concluded in an association of cancer to infectious agents, but such associations may be found with new tools and investigations.

Motion. A motion to concur on the Division of Cancer Control and Population Sciences' Program Announcement with special Receipt, Referral, and/or Review entitled "Co-Infection and Cancer" was approved unanimously.

XI. RE-ISSUE PARS—DR. PAULETTE S. GRAY

Dr. Paulette S. Gray, Director, DEA, presented 17 re-issue PARs for BSA consideration and noted that the list and a link to each PAR was made available on the secure BSA-only website prior to the meeting.

Dr. Gray reminded the BSA members that because of the large volume of PAR re-issues the NCI receives annually, the Board will review the re-issues as a group, not individually, and will vote to concur with the re-issuances. Dr. Gray indicated that metrics for evaluating the PARs discussed at the 25 March 2019 BSA meeting are being developed and will be addressed at a future meeting.

- Cognitive Science Research to Improve Assessment of Cognitive Impairment Following Cancer Treatment (PAR-18-605; PAR-18-606)
- Core Infrastructure Support for Cancer Epidemiology Cohorts (PAR-17-233)
- Fundamental Mechanisms of Affective and Decisional Processes in Cancer Control (PAR-18-681)
- Innovative Approaches to Studying Cancer Communication in the New Media Environment (PAR-18-638; PAR-18-639)
- Intervening with Cancer Caregivers to Improve Patient Health Outcomes and Optimize Health Care Utilization (PAR-18-246; PAR-18-247)
- Linking the Provider Recommendation to Adolescent HPV Vaccine Uptake (PAR-16-337; PAR-18-008; PAR-18-019)
- Mammalian Models for Translational Research (PAR-17-245)
- Mechanisms of Cancer and Treatment-Related Symptoms and Toxicities (PA-16-258)
- NCI Exploratory/Developmental Research Grant Program (Clinical/Translational Studies) (PAR-18-020)
- NCI Outstanding Investigator Award (PAR-18-880)
- Neural Regulation of Cancer (PAR-16-245; PAR-16-246)
- New Informatics Tools and Methods to Enhance U.S. Cancer Surveillance and Research (PAR-16-349)
- Perception and Cognition Research to Inform Cancer Image Interpretation (PAR-18- 640; PAR-18-641)
- Program to Improve the Rigor and Reproducibility of Exosomal Analytes for Cancer Detection (PAR-16-276; PAR-16-277)
- Revision Applications for Validation of Biomarker Assays Developed Through NIH-Supported Research Grants (PAR-17-003)
- Small-Cell Lung Cancer (SCLC): Biology, Therapy, and Resistance (PAR-16-049)
- U.S. Tobacco Control Policies to Reduce Health Disparities (PAR-18-674; PAR-18-675)

Motion. A motion to concur on the re-issue of PARs was approved unanimously.

XII. ONGOING AND NEW BUSINESS—DRS. ELIZABETH M. JAFFEE AND DAFNA BAR-SAGI

NCAB *ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities. Dr. Paskett, Chair of the NCAB *ad hoc* Population Science, Epidemiology, and Disparities Subcommittee, presented the report of the 9 June 2019 Subcommittee meeting. Dr. Paskett informed the Board members that the Subcommittee accepted the final report of the Working Group, which was presented earlier in today's meeting. The Subcommittee discussed the next charge for the Working Group and revisited the initial four focus areas identified by the former NCI Director, Dr. Sharpless. Dr. Paskett noted that focusing on health disparities likely will be the next topic for the Working Group.

Motion. A motion to accept the report of the 9 June 2019 NCAB a*d hoc* Population Science, Epidemiology, and Disparities Subcommittee meeting was approved unanimously.

NCAB Planning and Budget Subcommittee. Dr. Sawyers, Chair of the NCAB Planning and Budget Subcommittee, presented the report of the 9 June 2019 Subcommittee meeting. Dr. Sawyers referred the Board members to the detailed meeting summary contained in the Board book. He noted that

the Acting NCI Director, Dr. Lowy, informed subcommittee members of the NCI RPG Pool funding, the decreasing paylines, success rates, and the potential impact on overall RPG funding. Subsequently, Dr. Sawyers drafted a letter conveying the Subcommittee's concerns with the NCI's decreasing RPG Pool and relevant paylines and success rates relative to other ICs, which will be shared with Subcommittee members for input.

Motion. A motion to accept the report of the 9 June 2019 NCAB Planning and Budget Subcommittee meeting was approved unanimously.

Future Agenda Items/Other Business. The BSA and NCAB members were asked to forward any suggestions for potential future agenda items to Drs. Gray, Jaffee, or Bar-Sagi.

XIII. CLOSED SESSION - DR. ELIZABETH M. JAFFEE AND DR. DAVID CHRISTIANI

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).

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

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.

En bloc: The NCAB en bloc vote for concurrence with IRG recommendations was unanimous. During the closed session, a total of 2,696 NCI applications requesting direct cost support of $1,164,505,539 were reviewed.

XIV. ADJOURNMENT—DRS. ELIZABETH M. JAFFEE AND DAFNA BAR-SAGI

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 13th Joint meeting of the BSA/NCAB was adjourned at 5:42 p.m. on Monday, 10 June 2019.

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Date Dafna Bar-Sagi, Ph.D., Chair, BSA

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

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