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

6th VIRTUAL JOINT MEETING of the BOARD OF SCIENTIFIC ADVISORS AND NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
14-15 June 2022

Virtual Meeting
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
14–15 June 2022

The Board of Scientific Advisors (BSA) of the National Cancer Institute (NCI) and the National Cancer Advisory Board (NCAB) convened for the 6th Virtual Joint Meeting on 14–15 June 2022. The meeting was open to the public on Tuesday, 14 June 2022, from 1:00 pm to 3:49 p.m., and Wednesday, 15 June 2022, from 1:00 p.m. to 5:02 p.m., and closed to the public on Tuesday, 14 June 2022, from 4:05 p.m. to 5:29 p.m. The NCAB Chair, Dr. John D. Carpten, Professor and Chair, Department of Translational Genomics, Royce and Mary Trotter Chair in Cancer Research, Keck School of Medicine, University of Southern California; and BSA Chair, Dr. Keith T. Flaherty, Director Clinical Research, Massachusetts General Hospital Cancer Center, Professor of Medicine, Harvard Medical School, presided during the open sessions. Dr. Carpten presided during the closed session. In the open sessions, 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. Keith T. Flaherty (Chair)
Dr. Chandrakanth Are
Dr. Suzanne J. Baker
Dr. Karen M. Basen-Engquist
Dr. Michael John Becich
Dr. Mary C. Beckerle
Dr. Melissa L. Bondy
Dr. Otis W. Brawley
Dr. Andrew T. Chan
Dr. Nelson J. Chao (absent)
Dr. Gloria D. Coronado
Dr. Chyke A. Doubeni
Dr. Shelton Earp
Dr. Jennifer R. Grandis
Dr. Dorothy K. Hatsukami
Dr. Trey Ideker
Dr. Karen E. Knudsen (absent)
Dr. Michelle M. Le Beau
Dr. Karen M. Mustian
Dr. Sylvia Katina Plevritis
Dr. W. Kimryn Rathmell
Dr. Erle S. Robertson
Dr. Leslie L. Robison
Dr. Robert D. Schreiber
Dr. David Sidransky
Dr. Ian M. Thompson, Jr.
Dr. David A. Tuveson (absent)
Dr. Robert H. Vonderheide (absent)
Dr. Richard C. Zellars (absent)

NCAB Members

Dr. John D. Carpten (Chair)
Dr. Francis Ali-Osman
Dr. Nilofer S. Azad
Dr. Anna D. Barker
Dr. Luis Alberto Diaz, Jr.* (absent)
Dr. Howard J. Fingert
Dr. Christopher R. Friese
Mr. Lawrence O. Gostin (absent)
Dr. Andrea A. Hayes
Dr. Amy B. Heimberger
Dr. Scott W. Hiebert
Dr. Nikan Khatibi
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Margaret R. Spitz
Dr. Susan Thomas Vadaparampil
Dr. Ashani T. Weeraratna
Dr. Karen M. Winkfield

President's Cancer Panel

Dr. John P. Williams (Chair)
Mr. Robert A. Ingram (absent)
Dr. Edith P. Mitchell

*Pending appointment

Alternate *Ex Officio* NCAB Members

Dr. Michael A. Babich, CPSC (absent)
Dr. Gwen W. Collman, NIEHS
Dr. Joseph R. Graber, DOE
Dr. Michael Kelley, VA
Dr. Richard Pazdur, FDA (absent)
Dr. Tara A. Schwetz, NIH (absent)
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Douglas R. Lowy, Acting Director, National Cancer Institute
Dr. Oliver Bogler, Director, Center for Cancer Training
Dr. Philip E. Castle, Director, Division of Cancer Prevention
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Director, Division of Cancer Biology
Mr. Peter Garrett, Director, Office of Communications and Public Liaison
Dr. Katrina A.B. Goddard, Director, Division of Cancer Control and Population Sciences
Dr. Satish Gopal, Director, Center for Global Health
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
Dr. Tony Kerlavage, Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies McConville, Acting Director, Office of Scientific Operations, NCI at Frederick
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Dr. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program
Dr. Diane Palmieri, Acting Director, Center for Research Strategy
Dr. Henry Rodriguez, Director, Office of Cancer Clinical Proteomics Research
Mr. Jeffrey Shilling, Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Biomedical Informatics and Information Technology
Ms. Donna Siegle, Executive Officer and Deputy Director for Management, Office of the Director
Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development and Acting Director, Center for Strategic Scientific Initiatives
Dr. Sanya A. 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. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

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TUESDAY, 14 JUNE 2022

I. CALL TO ORDER AND OPENING REMARKS—DRS. JOHN D. CARPTEN AND KEITH T. FLAHERTY

Dr. John D. Carpten called to order the 6th Virtual Joint Board of Scientific Advisors (BSA) and National Cancer Advisory Board (NCAB) meeting. He welcomed members of the Boards, *ex officio* members, President's Cancer Panel 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. Dr. Carpten reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to accept the minutes of the 10 February 2022 NCAB meeting was approved unanimously.

Motion. A motion to accept the minutes of the 28–29 March 2022 BSA meeting was approved unanimously

Dr. Carpten called Board members' attention to the future meeting dates listed on the agenda, noting that the 2024 dates will need to be confirmed.

Motion. A motion to approve the 2024 NCAB meeting dates was approved unanimously.

Motion. A motion to approve the 2024 BSA meeting dates 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 6th Virtual Joint Meeting of these Boards and reviewed the agenda. He provided an update on leadership transitions, the NCI budget, cancer equity, and cancer research advances. Dr. Lowy began by reflecting on the life and career of John Edward Porter, Illinois 10th district Congressman from the mid-1980s until 2001, who passed away on 3 June 2022. Mr. Porter, a strong supporter of the NIH, is attributed with doubling the NIH budget in the late 1980s and early 2000s. After leaving Congress, Mr. Porter served as chairman of the board of directors of Research!America, from 2005 until his passing. The NIH John Edward Porter Neuroscience Research Center, dedicated in 2014, is named after him. Dr. Lowy remarked that Mr. Porter was a bipartisan member of Congress and a true champion for biomedical research and other causes, including gun control.

Dr. Lowy congratulated NCAB and BSA members on their recent awards. 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, is recipient of the 2022 American Society of Clinical Oncology (ASCO)–American Cancer Society Cancer Prevention Award; Dr. Karen M. Winkfield, Executive Director, Meharry-Vanderbilt Alliance, Ingram Professor of Cancer Research, Professor of Radiation Oncology, Vanderbilt University School of Medicine and Dr. Otis W. Brawley, Bloomberg Distinguished Professor of Oncology and Epidemiology, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, are selected 2022 Fellows of the American Society of Clinical Oncology; and Dr. Jennifer R. Grandis, Robert K. Werbe Distinguished Professor in Head and Neck Cancer, University of California, San Francisco, is in the class of 2022 Fellows of the American Association for Cancer Research (AACR) Academy.

NCI Leadership History, Transitions, Decisions, and Activities. Dr. Lowy reminded the BSA and NCAB members of the NCI directors over the past decade. Dr. Harold E. Varmus was the director

from 2010 to 2015. Dr. Lowy was acting director from 2015 to 2017. Dr. Norman E. Sharpless was director from 2017 to 2022 and also served as U.S. Food and Drug Administration (FDA) Acting Commissioner from 1 April to 6 November in 2019, during which time Dr, Lowy served as NCI Acting Director. In May 2022, Dr. Lowy again became NCI Acting Director following Dr. Sharpless' announcement that he would step down effective 30 April 2022. Dr. Lowy acknowledged the NCI senior leadership team, noting that this team has remained unchanged over the years, and they support whoever is the NCI director.

Dr. Lowy noted some of the decisions of 2015 to 2019 that have occurred during his previous tenures as acting director. In 2015, the Precision Medicine Initiative in Oncology launched and the National Cryo-Electron Microscopy Facility (NCEF) opened. In 2016, the Cancer Moonshot℠ was approved under the 21st Century Cures Act, and the NCI implemented a more than $40 million (M) increase (phases 1 and 2) in the NCI-Designated Cancer Centers (Cancer Centers) Support Grants (CCSGs, P30) that is continuing into 2022. In 2019, the Institute enabled Congress to better understand the low NCI funding rates for investigator-initiated research.

Regarding current and future NCI activities, the Cancer Grand Challenges program, a collaboration with Cancer Research United Kingdom, will announce winning multidisciplinary teams on 16 June 2022. NCI staff will participate in the development and process for the next phase of the Cancer Moonshot, and Dr. Lowy noted that the NCI will need to continue to fund the most promising initiatives of the initial phase. In 2023, the NCI will develop phase 3 of the CCSGs and will select a new signature project for the Frederick National Laboratory for Cancer Research (FNLCR). To facilitate this FNLCR activity, NCI and FNLCR staff, led by Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development and Acting Director, Center for Strategic Scientific Initiatives, and Dr. Edward Harlow, Special Advisor to the NCI Director, have been conducting meetings to solicit ideas and suggestions, in addition to issuing a request for information (RFI) in 2021.

Just prior to being named acting director, but after Dr. Sharpless' announcement of his departure, Dr. Lowy attended the April 2022 AACR Remarks and Fireside Chat and a press briefing with AACR outgoing President and BSA member Dr. David Tuveson and the April 2022 National Association of Cancer Center Development Officers–Public Affairs and Marketing Network meeting. He recently attended and presented a plenary speech at the June 2022 ASCO Annual Meeting and met with the ASCO Board of Directors. In October 2022, he plans to attend the Annual Association of American Cancer Institutes (AACI) meeting.

NCI Budget. On 11 May 2022, Dr. Lowy participated in the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS) hearing. He remarked on the continued bipartisan support for the NIH and the NCI and noted that he has maintained long-standing relationships with congressional leaders. Dr. Lowy noted that Ms. M.K. Holohan, Director, Office of Government and Congressional Relations (OGCR), NCI, will provide further details on the NCI fiscal year (FY) 2023 budget later in the meeting. Members were reminded that typically, the President's budget proposal has been lower than the expected appropriations, which Dr. Lowy attributed to strong bipartisan support for cancer research across Congress and the appropriators' declining to cut funding in this area, even in challenging budget cycles. Dr. Lowy conveyed his optimism for similar outcomes for FY 2023 that will come because of the cancer community's emphasizing to Congress the importance of funding cancer research and of the NCI for helping patients and for preventing and treating cancer.

Cancer and Health Equity. On 8 June 2022, the NCI hosted a live virtual conversation about equity in the health care workforce. Drs. Lowy and Paulette Gray moderated the session. Panelists included Dr. Jeffrey Hall, Deputy Associate Director for Science, Centers for Disease Control and Prevention (CDC), and Dr. Randy A. Jones, Professor at the School of Nursing, University of Virginia,

and representative for the Oncology Nursing Society. This event commemorated the 2022 Juneteenth holiday, and the recordings can be accessed via the NCI social media channels: youtube.com/NCIgov and facebook.com/cancer.gov.

Dr. Lowy called attention to national trends in mortality over the last 20 years, stratified by race and ethnicity. According to NCI Surveillance, Epidemiology, and End Results (SEER) Program data, the age-adjusted cancer mortality decreased across all groups, with the highest decline in African American/Black men. Although these decreases have been notable, Black/African American men and women continue to have higher mortality rates than other groups. In addition, American Indian and Alaska Native men have not benefited from the advances in cancer research to the same degree as other ethnic groups. Members were directed to the recent report in the 19 May 2022 issue of *JAMA Oncology* for further information on this topic.

Dr. Lowy elaborated on contributing factors to the decrease in cancer mortality rates. The first reason is the decline in lung cancers, which account for a third of all mortality from cancer. Evidence has shown that tobacco consumption is the major cause of lung cancer and, to a lesser extent, other cancers. The second reason is that other factors are fueling the decrease in lung cancer incidence and mortality, including advances in lung cancer treatment, particularly targeted therapy, and immunotherapy for non–small cell lung cancers. The Lung Cancer Research Foundation illustrates on its website the effects of the increasing rate of FDA approvals for lung cancer treatment, and NCI intramural investigators published a report in the 13 August 2020 issue of the *New England Journal of Medicine* emphasizing that lung cancer treatment is having a substantial effect population-wide in the United States.

Cancer Research Progress. Dr. Lowy reported on recent intramural and extramural cancer research progress. The advances in treating RAS (a family of genes mutated in more than 30% of cancers) mutations (e.g., KRAS) in people with cancer have been significant. These mutations were first identified in the early 1980s, when Dr. Lowy and his laboratory and collaborators identified the first KRAS codon 12 mutation. Over the next 30 years of research, RAS was considered an intractable mutant challenge, without any promising treatments. Advances pioneered by Dr. Kevan M. Shokat at the University of California, San Francisco (UCSF) and his collaborators have enabled the first inhibitor of the KRAS mutant G12C (sotorasib) to achieve FDA approval in May 2021. A recent review conducted by Dr. Frank McCormick, RAS National Program Advisor, and Professor Emeritus, UCSF, and NCI RAS Initiative program investigators on the number of new cancer cases per year in the United States that contain the most frequent KRAS mutant alleles revealed the G12C mutation to be the most common in lung cancers. Preclinical data support the development of inhibitors for G12D, a KRAS mutation prevalent in pancreatic cancers. Early phase clinical trials will start soon. The NCI Patient-Derived Models Repository (PDMR) currently contains a wide range of patient-derived xenografts (PDX) and other cancer models, including G12C PDXs. These resources are available to the cancer research community.

Recent data reported in the 5 May 2022 issue of *JAMA Oncology* revealed that uterine cancer death rates are increasing and are highest among Black/African American women in the United States, who are twice as likely to die of uterine cancer than other racial and ethnic groups. Most of this mortality increase is attributable to non-endometrioid uterine cancer, which disproportionately affects Black/African American and Hispanic women. In fact, between 2010 and 2017, non-endometrioid cancer mortality increased 3.5 percent annually in Black/African American women and 6.7 percent in Hispanic women. These data emphasize an urgent need for new research on the affected populations. The NCI is planning to schedule two internal discussions to consider what research should be conducted to better understand these findings.

Dr. Lowy highlighted preliminary results of the Anal Cancer High-grade Squamous Intraepithelial Lesions [HSIL] Outcomes Research (ANCHOR) Study. Observations showed that

treatment of HSIL reduces the risk of progression to invasive anal cancer in patients testing positive for HIV. The ANCHOR Study report is to be published in the 16 June 2022 issue of the *New England Journal of Medicine*.

Cancer Moonshot Updates. Members were reminded of the overarching goals of the initial Cancer Moonshot: to accelerate discovery, increase collaboration, and expand data sharing. From 2017 to 2021, investigators produced 2,000 publications, launched 49 clinical trials, and filed more than 30 patent applications. FY 2023 marks the last year of funding for the initial Cancer Moonshot. Dr. Lowy remarked that the NCI strives to continue to support the most promising initiatives while developing additional activities to meet challenging new goals.

On 2 February 2022, President Joseph R. Biden announced three critical aspirational goals of the reignited Cancer Moonshot, to: (1) decrease the national cancer death rate by half within the next 25 years, (2) transform the meaning of cancer, and (3) address cancer-associated inequities. The NCI is playing a critical role in helping to make these aspirational goals feasible. Four overarching approaches are to: (1) invest in the pipeline of new drugs for cancer prevention, interception, and treatment; (2) expand clinical trials to speed evaluation of candidate interventions in diverse populations; (3) ensure equitable health care delivery of current and new standards of care; and (4) increase the diversity of cancer research and the cancer care workforce to make it more closely resemble the communities that we serve.

In FY 2023, the NCI is planning to support the next phase of the Cancer Moonshot through several activities. Dr. Lowy informed members that, later in today's meeting, NCI staff will present two proposed funding opportunity announcements (FOAs) that will be foundational. The FOAs will focus on a scholars diversity program for early-stage investigators (ESIs) and a feasibility trial for asymptomatic multi-cancer early detection (MCED) and screening. In addition, the NCI plans to issue notices of special interest (NOSIs) and RFIs for existing projects, including adapting visualization methods to enhance Cancer Moonshot data and fusion oncoproteins in childhood cancers.

Questions and Answers

NCAB Chair Dr. Carpten asked about the next FNLCR initiative and inquired about updates on NCI's ongoing interactions with the FNLCR. Dr. Lowy noted that the FNLCR has been heavily supporting COVID-19-related activities, both at the NCI and National Institute of Allergy and Infectious Diseases (NIAID). Regarding cancer research activities, the RAS Initiative, in its ninth year, has distributed several reagents and resources to the cancer community and soon will be undergoing its third renewal. He also stated that the virtual 2021 RAS Initiative Symposium attracted more than 1,500 participants. The next symposium is planned for October 2022 as an in-person event at NCI at Frederick. In addition, Dr. Lowy noted that the NCI launched the PDMR, spearheaded by Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, NCI and has been considering the next large-scale FNLCR project. Members were informed that the FNLCR-managed NCEF has been successful. Dr. Singer added that the NCI released an RFI in 2021 soliciting input from the cancer research community on a next FNLCR project and, subsequently, has convened nine think tanks, inviting a broad range of the cancer research community to participate. Other smaller focused meetings are planned. The NCI will synthesize the common themes and develop ideas that could then be considered by the Boards within the next year.

Dr. John P. Williams, Breast Cancer Surgeon, Medical Director, Breast Cancer School for Patients, Clinical Professor, Institute for Biohealth Innovation, George Mason University, asked about NCI's role in the reignited Cancer Moonshot and engagement with the new Cancer Cabinet. Dr. Lowy stated that President Biden announced a whole-of-government approach to addressing cancer and achieving the new goals previously described and has convened meetings. The Cancer Cabinet, composed of deputies assigned from across federal agencies, including former NCI Director Dr. Sharpless, has

attended and participated in those meetings. Other NCI leadership, including Drs. Lowy, Singer, and Doroshow, have participated in the activities. Dr. Danielle Carnival, coordinator for the next phase of the Cancer Moonshot, has been leading these efforts. A recent meeting on clinical trials included patient advocates and Cancer Center representatives discussing the importance of accruing more patients for trials and doing so equitably. The NCI anticipates making rapid advances in cancer prevention, screening, and treatment. Because patient accrual and, in particular, equitable accrual are critical to making the advances, the expectation is that these efforts will lead to new standard-of-care or implementation research to improve dissemination.

Dr. Chyke A. Doubeni, Professor of Family Medicine, Center for Health Equity and Community Engagement Research, Mayo Clinic Cancer Center, Center for Clinical and Translational Science, Mayo Clinic, remarked on an equity-in-all approach to cancer research and research in general, and asked to what extent could such conversations be integrated to provide a framework for core efforts. To make advances in cancer and any other condition, Dr. Doubeni remarked, a field would need to advance equity, extending benefits to every group in a society. Dr. Lowy commented that NCI's primary role in health care delivery is to support implementation science research. Dr. Carnival and others at the Office of Science and Technology Policy (OSTP) are promoting equity for health care delivery beyond implementation research. At the level of clinical trials, the NCI ensures that trial participants reflect the communities being served. In addition, with the proposed Cancer Moonshot Scholars program that the BSA will be evaluating later in the meeting, as well as other programs at the Center to Reduce Cancer Health Disparities (CRCHD), the NCI is helping shape the work force of tomorrow so that it more reflects the general community.

In response to a question from Dr. Doubeni about inclusivity across all spheres of research and whether inclusive research would be emphasized across the NCI, Dr. Lowy noted that implementation research includes a wide range of populations and underrepresented groups. The NCI wants basic researchers to be more equitably distributed, not because health disparities were being neglected but because equity has become an important consideration.

Dr. Anna D. Barker, Chief Strategy Officer, Ellison Institute for Transformative Medicine, University of Southern California, asked about plans to further enhance data sharing efforts and build the Cancer Research Data Commons (CRDC) for the next phase of the Cancer Moonshot. Dr. Lowy explained that the goal of pediatric cancer research is for all children with cancer to have their data deposited into a repository that will be available to the research community. The appropriate consent agreements must be in place. The aim is that pediatric cancer centers from other countries will participate in data sharing with the NCI. The process of adding a large database to the cloud to enable multi-omics analysis beyond the Genomic Data Commons (GDC) is in progress. Dr. Singer added that the initial phase of the Cancer Moonshot required that data from the funded studies be open and accessible immediately upon publication. The NCI supported improvements in the CRDC to allow common data standards and interoperability and more recently discussed these standards in the context of clinical data, which is complicated to address.

Dr. Michelle M. Le Beau, Arthur and Marian Edelstein Professor Emerita of Medicine, Director Emerita, University of Chicago Comprehensive Cancer Center, Chief Scientific Officer, Cancer Prevention and Research Institute of Texas, sought clarity on the clinical trials update during this meeting. Dr. Lowy clarified that the NCI would discuss MCED and screening and a related study but will not have a clinical trials update.

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

Ms. Holohan provided a report on FY 2023 appropriations, pending legislation to monitor, and the congressional calendar. She called attention to the detailed legislative report in the Board meeting book. Ms. Holohan reminded attendees of the process through which NCI receives its appropriation. The

FY 2022 omnibus bill was not enacted until March 15—almost halfway through the fiscal year—delaying many other events, such as the President's budget, which was released in late March rather than early February. Subcommittees have held appropriations hearings and currently are drafting bills; the House Appropriations Committee plans to mark up all bills by the end of July. Appropriators held hearings on the NIH budget in mid-May. Ms. Holohan pointed out that Congress has been gathering testimony from cancer researchers and patients, and they also have heard testimony about diversity in clinical trials as part of a larger hearing on several health bills.

Ms. Holohan clarified that the NIH was funded with a continuing resolution, which maintained funding at FY 2021 levels, until mid-March, and this level was used as the baseline for the FY 2023 budget calculation. However, NCI's FY 2022 budget included a $353 million increase, so the FY 2023 budget appears to propose a $199 million cut. Ms. Holohan pointed out that 11 other Institutes and Centers have similar differences between the FY 2023 budget request. Acting NIH Director Dr. Lawrence Tabak published a blog post to explain that the administration's intent was not to reduce funding. Ms. Holohan emphasized that Congress has consistently declined to cut funding for cancer research, even during challenging budget cycles.

The House recently adopted a deeming resolution instead of a budget resolution. This type of resolution sets the top-line discretionary spending numbers, which in this case results in a 9 percent increase from the previous year, and it enables appropriators to begin moving bills in the House. However, the deeming resolution does not resolve some of the challenges that tend to delay budget approval, such as the balance between defense and non-defense spending or give allocations to subcommittees. Ms. Holohan commented that appropriation action likely would not occur until after the midterm elections. FY 2023 appropriations may be moved into the next Congress, although disincentives for that action include a desire for new committee leadership to start fresh and a desire for retiring leadership to deliver earmarks for their constituents.

Ms. Holohan noted that the Advanced Research Projects Agency for Health (ARPA-H) is continuing to develop, but many questions remain from authorizers and appropriators. In FY 2022, appropriators provided $1 billion in funding for ARPA-H that can be spent over 3 years, which was distributed in April. Because the final form of ARPA-H remains undetermined, the appropriations bill allowed U.S. Department of Health and Human Services (HHS) Secretary Xavier Becerra to direct that money anywhere within HHS, including the NIH, which allows existing NIH infrastructure to be used for ARPA-H projects. The President's FY 2023 budget request included an additional $4 billion for ARPA-H, and although three authorizing bills have been drafted, none were completed before FY 2022. Each of the draft bills used different approaches to ARPA-H's potential relationship with the NIH. The last report from the House is that members are working together to coordinate their approach; the Senate bill specifies that the new agency cannot be located in the Capital area and prohibits ARPA-H from hiring people who have been employed by the NIH within the previous 3 years. Ms. Holohan pointed out that ARPA-H can continue in its current form, funded by the previous appropriation, and her team will be watching further developments closely.

Some authorizations are expiring and must pass within a short time frame, including the FDA User Fee Reauthorization; the Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) program; and the National Defense Authorization Act (NDAA), which sets a top-line funding goal for the defense program. The discussion of the NDAA will involve consideration of how to portion defense and non-defense spending. One of the administration's additional priorities is the American Competitiveness Legislation, on which more than 100 members of Congress are conferencing to resolve the House and Senate versions. Ms. Holohan theorized that another attempt to pass the Build Back Better Reconciliation Package may occur, which would advance some important domestic administration priorities. If that package can be acted on before the end of September, it could be passed

with a simple majority. She also suggested that another attempt at passing COVID-19 funding may occur. Other bills could be attached to the three expiring bills as riders to move other administration priorities.

Ms. Holohan showed that only 30 days remain in which the House and Senate are both in session, and many members are busy campaigning for reelection; additionally, some key nominations require time in the Senate calendar. Nominees have not been announced for the position of NIH Director or OSTP Director, both of which require Senate confirmation. The midterm elections are likely to be volatile and unpredictable. The next Congress will include many new members given the number of current members who are retiring, including several senior appropriators and long-time NIH champions in the Senate, as well as several strong cancer research advocates in the House. She noted that the biomedical research champions remaining in Congress have renewed action to engage with the NIH, particularly during the difficult circumstances surrounding the COVID-19 pandemic.

Questions and Answers

NCAB Chair Dr. Carpten asked when the APRA-H funds would expire. Ms. Holohan explained that the funds are available for 3 years, which provides particular flexibility for ARPA-H as a new entity not funded until late in the fiscal year.

Dr. Barker asked for clarification on ARPA-H focus areas and funding processes. Ms. Holohan explained that appropriators expect ARPA-H to focus on certain disease areas, including cancer, amyotrophic lateral sclerosis (ALS), diabetes, and Alzheimer's disease. She expects that those focus diseases will not change, but many unknowns remain about how the organization will work and how funding will be made available. She directed interested parties to a recent presentation by NIH Acting Principal Deputy Director, Dr. Tara A. Schwetz, to the NIH Advisory Committee to the Director, which provided as much detail as is currently available. When asked who will lead ARPA-H, Ms. Holohan explained that a deputy director has been appointed, but she is not aware of any additional leadership candidates. Regarding project managers, Ms. Holohan noted that a 3-year cap for project managers has been discussed, but additional details have not been defined.

Dr. Christopher R. Friese, Elizabeth Tone Hosmer Professor of Nursing, Director, Center for Improving Patient and Population Sciences, Associate Director for Cancer Control and Population Sciences, University of Michigan Rogel Cancer Center, University of Michigan, suggested that the research community is looking for clarity to be able to engage meaningfully with ARPA-H and develop good science. He encouraged attendees who may be asked to contribute to ARPA-H to keep this point in mind.

IV. PRESIDENT'S CANCER PANEL REPORT: CLOSING GAPS IN CANCER SCREENING—DR. JOHN P. WILLIAMS

Dr. Williams, the chair of the President's Cancer Panel (Panel or PCP), provided an update on the Panel's recent report issued with the Cancer Moonshot titled "Closing Gaps in Cancer Screening: Connecting People, Communities, and Systems to Improve Equity and Access." The three-member panel was established by the National Cancer Act of 1971 to monitor the development and execution of the activities of the National Cancer Program and report directly to the president, and its main activity is identifying high-priority topics for which actionable recommendations can be made. Dr. Williams noted that the Panel does not distribute funds or have particular power, its role is to prepare a report to encourage stakeholders, including the BSA and NCAB, to take action.

Cancer screening rates plummeted during the COVID-19 pandemic, and at one-point screenings were reduced by 90 percent. The long-term impact of missed or delayed screenings will be increased morbidity and mortality from cancer. Even before the COVID-19 pandemic, cancer screening uptake was incomplete and uneven. Significant gaps exist between recommended cancer screening and uptake, as

well as lack of timely follow-up after an abnormal test result. Such gaps are more common in many communities of color, socially and economically disadvantaged populations, those with low educational achievement, and populations residing in certain areas of the country. Barriers include lack of awareness and understanding, lack of provider recommendation, logistical challenges, fear and stigma, and cost.

Four working groups have been convened to close gaps in screening for lung, colorectal, cervical, and breast cancers. The working groups met virtually over the summer of 2020 to identify critical barriers and opportunities for each of these tumor types, then the PCP convened a series of public meetings, bringing together more than 160 stakeholders to discuss cancer screening during the COVID-19 era. The first series, in fall 2020, focused on barriers to and opportunities for breast, cervical, colorectal, and lung cancer screening. The meetings held in winter 2021 focused on innovations in cancer screening.

Dr. Williams outlined four goals related to closing gaps in cancer screening: (1) improve and align communication, (2) facilitate equitable access, (3) strengthen workforce collaborations, and (4) create effective health information technology (IT). He encouraged attendees to read the entire report for more information. One common theme across all four tumor types is the need for better communication around the opportunities and benefits of cancer screening, as well as the harms. Effective communications that reach all populations need to be developed, and information that empowers people to make decisions and take action should be developed and disseminated. The report recommended leveraging the National Cancer Roundtables, creating roundtables for breast and cervical cancer, and increasing funding for colorectal and lung cancer roundtables. The Panel also recommends prioritizing equity and aligning messaging.

To facilitate equitable access, Dr. Williams noted that "high touch" strategies are needed to reach the under-screened and build relationships with communities that have difficulty accessing cancer screenings. He added that sustainable funding is needed for community-oriented outreach and support, including community health workers. Access to self-sampling also should be increased through stool-based testing for colorectal cancer screening and human papillomavirus (HPV) self-tests for cervical cancer screening.

Workforce collaborations in health care settings can be strengthened. Providers have competing demands and difficulty thoroughly addressing all needs during a short visit. All members of the health care team should be empowered to support cancer screening through improved policies, systems, and team-based approaches. The requirement for shared decision-making in lung cancer is the best opportunity to identify people who are in a curable stage of cancer, but the physician one-on-one requirement can be a barrier; the Panel recommends that, despite the risk of over-screening, this process should become team oriented. Additionally, access to genetic testing for cancer risk assessment should be expanded—all those eligible should be offered genetic testing with informed consent, and genetic counselors should be recognized as health care providers by the Centers for Medicare & Medicaid Services (CMS).

Effective health IT is needed because large amounts of constantly changing information—such as family history, multiple electronic health records, and screening guidelines—must be processed for cancer screening and follow-up. Improved health IT can allow providers and health care systems to access clinical knowledge and patient data more efficiently with computable guidelines and effective clinical decision support tools.

Dr. Williams emphasized the need to work together to close the gaps in screening. A multipronged approach is critical to support people, communities, and systems for cancer screening and follow-up after an abnormal result, and this approach should include access, communications, and implementation. He pointed out that implementing existing cancer screening guidelines more effectively and equitably can make a difference immediately.

The PCP Report and Cancer Moonshot reignition were released together on February 2, 2022. The report release coincided with President Biden's recommitment to the Cancer Moonshot, including a call to action on cancer screening and early detection as one of the OSTP priorities. Many of the recommendations were implemented rapidly. The American Cancer Society announced that it would launch a National Breast Cancer Roundtable and National Cervical Cancer Roundtable, and the National Lung Cancer Roundtable initiated a summit to accelerate lung cancer screening, which will be held in Washington, D.C., in July. Additional stakeholder implementation activities include the creation of the "Cancer Cabinet" and identification of screening improvement initiatives in many sectors.

Questions and Answers

Dr. Brawley pointed out that lung cancer screening has been shown to save 5.4 lives for every death caused as the result of an invasive procedure caused by the screening, and a third of those who die do not have cancer on autopsy. He asked how to maintain that high ratio when screening is implemented in places other than the best hospitals in the country. Dr. Williams acknowledged the harms of invasive screening but pointed out that the roundtable model includes experts at many levels of the process and expressed confidence that the National Lung Cancer Roundtable can find a shared decision-making model that will minimize the harms of cancer screening.

Dr. Andrea A. Hayes, Professor and Chair, Department of Surgery, Howard University, Washington, D.C., asked about the efforts to expand screening through education. Dr. Williams explained that addressing inequitable screening in many diverse communities and populations requires translating messaging appropriately for smaller groups in many geographic locations. He pointed out that the experts in the roundtables can help tailor messages to the specific communities they represent.

Dr. Paskett commented that unlike community health workers, patient navigators cannot be reimbursed, and emphasized the need to fund patient navigators, whose services are essential for increasing screening, addressing disparities, and tailoring messages to specific populations. She added that cervical cancer survival rates are decreasing despite its preventability. Dr. Williams agreed that patient navigation plays a significant role but noted that community health workers were highlighted in the report because of their ability to reach diverse communities. He noted that self-sampling for HPV can improve screening for cervical cancer.

Dr. Susan Thomas Vadaparampil, Associate Center Director, Community Outreach, Engagement, and Equity, Professor, Department of Health Outcomes and Behavior, Moffitt Cancer Center, recommended emphasizing NCI's repository of evidence-based interventions that are available for communicating with diverse audiences.

V. MYELOID MALIGNANCIES: THE JOURNEY FROM BASIC MOLECULAR BIOLOGY TO CLINICAL APPLICATION—DR. DAVID R. LARSON

Dr. Daniel R. Larson, Head, Systems Biology of Gene Expression, Laboratory of Receptor Biology and Gene Expression, Co-Director, Myeloid Malignancies Program (MMP), Center for Cancer Research (CCR), NCI, described the new NIH-wide MMP. He explained that the MMP has a specific emphasis on myelodysplastic syndromes (MDS), a clonal hematopoietic stem cell disease in which bone marrow cells have an abnormal distribution of cell types and morphology. MDS leads to profound cytopenia and has the potential to transform to secondary acute myeloid leukemia (AML). About 30,000 MDS cases are reported in the United States each year; 10 to 20 percent of cases are therapy related, and 80 to 90 percent arise *de novo*.

Germline predisposition to MDS has been increasingly recognized, particularly in children and younger adults. Treatment options include supportive care options to achieve hematological improvement. The only drug that has been approved for MDS in the past two decades, however, is

luspatercept, which is prescribed to patients who do not respond to other erythroid-stimulating regimes. Allogeneic stem cell transplant is the only cure for MDS, but this procedure is difficult to conduct in patients with comorbidities. Dr. Larson noted that the mortality of MDS is similar to that of lung cancer across stages. He explained that his presentation would feature studies involving investigators from multiple NIH Institutes and Centers. He emphasized that clinical activities involving MDS fall within NCI's purview because of the preponderance of somatic mutations in the disease, its propensity to transform to AML, and its mortality profile.

Barriers to progress in MDS research include limited understanding of disease biology and a dearth of animal and cellular models, lack of developed methods and definitions of measurable residual disease to guide therapies, and the fact that many patients with MDS are elderly and present with comorbidities. Progress on the development of MDS therapeutics has stalled in the past 15 years. MDS represents a unique disease model to study *in situ* evolution of cancer from inflammation, as well as genetic defects in disease manifestation. Dr. Larson noted that MDS is particularly relevant for many intramural programs within the NCI (e.g., RNA Biology Initiative). The disease's subacute clinical course is suitable for outpatient management. An opportunity exists to study MDS in a coordinated, multi-Institute approach across protocols and in both children and adults. Efforts will include nucleating activities in both intramural and extramural communities; convening the broader MDS scientific community; and mobilizing resources for trials, biomarker development, and preclinical models. Dr. Larson added that this work could help inform timing of hematopoietic stem cell transplantation.

MMP's mission is to develop a comprehensive program aimed at understanding and treating myeloid malignancies in children and adults. The Program's vision is to successfully control, cure, and ultimately prevent MDS and AML. The MMP was established in 2020 following an exploratory seminar series and organizational planning and establishment of milestones, and recruitment of staff was initiated in 2021. The MMP is based on four themes: (1) post-transcriptional regulation in MDS and AML, (2) germline predispositions to myeloid malignancy, (3) preclinical models to study MDS biology and therapy, and (4) the role of the immune system in control of MDS and AML. The Program is led by Dr. Steven Pavletic, Senior Clinician, Immune Deficiency Cellular Therapy Program, CCR, NCI, and involves representatives from additional NIH Institutes and Centers, including the National Heart, Lung, and Blood Institute (NHLBI); National Human Genome Research Institute; and NIH Clinical Center.

Theme 1 focuses on post-transcriptional regulation in MDS and AML. Dr. Larson explained that his work is most closely aligned with this theme. MDS mutations in splicing machinery were discovered in large-scale cancer sequencing studies that were published in 2011 and 2012. The first spliceosome structure was solved in 2015. Since that time, a revolution has occurred in the structural understanding of the spliceosome. Therefore, the spliceosome is a promising target in MDS research. Dr. Larson's research is focused on developing cutting-edge approaches for understanding transcription splicing and gene regulation in single cells (e.g., nascent RNA sequencing, single-molecule imaging, splicing and transcription). His group discovered that U2AF1 plays a non-canonical role in the translational regulation; cytokine interleukin-8 (IL-8) was one of the main targets that was mis-regulated by this mechanism. In collaboration with Dr. Christopher Hourigan, Senior Investigator, Myeloid Malignancies Section, NHLBI, Dr. Larson found that more than 30 percent of relapsed AML patients exhibited splicing factor mutations, as well as high levels of IL-8. In a lung xenograft model, the group blocked tumor progression using neutralizing antibodies to IL-8. The group partnered with Bristol Myers Squibb and received FDA investigational new drug (IND) approval in September 2021.

Theme 2 focuses on germline predispositions to myeloid malignancy. Dr. Larson emphasized that the NIH has established a long-standing track record of success in performing natural history studies and studying patients with germline predispositions. He highlighted recent work by Dr. Lea Cunningham, Associate Research Physician, Immune Deficiency Cellular Therapy Program, CCR, NCI. Dr. Cunningham hypothesized that imatinib can enhance wild-type RUNX1 protein activity in

RUNX1-deficient patients, potentially improving megakaryocyte dysplasia, thrombocytopenia, platelet dysfunction, and autoinflammation. This mechanism also could decrease the acquisition of secondary somatic mutations and slow or prevent the development of MDS and AML in affected individuals.

Theme 3 focuses on preclinical models to study MDS biology and therapy. Dr. Larson highlighted the work of Dr. Peter Aplan, Senior Investigator, Genetics Branch, CCR, NCI. Dr. Aplan's group developed an MDS mouse model that was used for the approval of luspatercept. Dr. Larson emphasized that Dr. Aplan's work has produced one of the few existing preclinical models for MDS.

Theme 4 focuses on the role of the immune system in control of MDS and AML. Dr. Larson noted that a trial for a first-in-human and first-in-child CD33 CAR T-cell therapy is being led by NCI CCR investigator Dr. Nirali Shah. He noted that CD123 and CD33 have been identified as potential therapeutic targets in the control of AML; in particular, CD33 is considered a less risky target for a first CAR T-cell therapy for this disease. Dr. Larson emphasized that this effort reflects a collaboration among the NCI, Children's Hospital of Philadelphia, and the University of Colorado.

MMP's first goals were to form an MDS/AML clinic as a site to study the disease presentation and biology and to develop assessment tools and pursue enrollment on clinical therapy protocols. The group has focused on recruiting a clinical translational team of physician scientists, clinical research fellows, a staff clinician, and research nurses. Additionally, several clinical trials have been initiated. Dr. Larson added that the MMP also is focused on recruiting basic scientists and engaging NIH investigators from relevant fields. Dr. Larson briefly highlighted recent work involving bispecific T-cell engagers, which could allow localized, controlled target killing with T cells potentially infused at a lower dose. He emphasized that multiple therapies are in development, and the program will focus on evaluating their effectiveness. He also highlighted the Molecular Evaluation of AML Patients After Stem Cell Transplant to Understand Relapse Events (MEASURE) protocol, which is being developed to develop a logistical framework for harmonized testing across major transplant centers. MEASURE will be launched in August 2022.

Questions and Answers

Dr. Le Beau remarked that a number of national and international consortiums and foundations already are working on MDS. She wondered about opportunities for the NCI to interact with these efforts. Dr. Larson agreed that foundations and patient advocates are critical to the MMP's outreach and referral efforts, and he noted that professional organizations have engaged in previous symposia. He added that the MMP is focused on unique unmet needs in MDS. In a follow-up comment, Dr. Le Beau inquired about NCI's interest in preventive tools to reduce the risk of chronic inflammation. Dr. Larson responded that his group's work has focused on inflammatory changes with MDS, and several intramural investigators possess expertise on this topic.

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology, Professor Emeritus of Neurosurgery, Duke University Medical Center, spoke on an MD Anderson clinical trial involving inhibitors of GSTP1, which might be involved in inflammatory processes that are associated with the MDS. Dr. Larson responded that he was unaware of the trial but that MMP is interested in cytokine profiling, as well as proteomics of inflammatory pathways.

Dr. Amy B. Heimberger, Jean Malnati Miller Professor of Brain Tumor Research, Vice Chair for Research, Department of Neurosurgery, Northwestern University Feinberg School of Medicine, noted that AstraZeneca has been involved in preclinical research using xenograft models in studies of AZD9150. She asked about pipeline selection and use of companion biomarkers. Dr. Larson explained that a steering committee will prioritize protocols. Areas for consideration include unique contributions to biological questions, as well as the development of a clinical trials portfolio for patients. He noted that a retreat will be held in the summer for further conversation on this topic.

VI. HUMAN TUMOR ATLAS NETWORK (HTAN) UPDATE—DRS. ETHAN CERAMI, MARTHA J. SHRUBSOLE, AND JOE W. GRAY

Data Coordinating Center (DCC). Dr. Ethan Cerami, Director, Knowledge Systems Group, Principal Scientist, Department of Data Science, Dana–Farber Cancer Institute, presented an overview of the HTAN DCC. He explained that HTAN is a collaborative network composed of 10 research centers, a pilot precancer project, and a pilot cancer atlas project. The HTAN is focused on understanding the molecular basis of transitions in cancer. Most HTAN groups have a strong focus on single-cell analysis, as well as multiplex imaging modalities, and the research groups are generating rich longitudinal data sets. More information can be found at the HTAN website or in the 16 April 2020 issue of *Cell*.

The DCC spans the Dana–Farber Cancer Institute, Sage Bionetworks, Institute for Systems Biology, and Memorial Sloan Kettering Cancer Center, and a collaboration is maintained with Harvard Medical School. DCC's mission is to develop data standards and enable data integration and to facilitate sharing and visualization of all HTAN data. Dr. Cerami explained that the DCC is focused on defining atlases by considering clinical data, biospecimens, molecular profiling approaches, and imaging modalities. HTAN also is focused on ensuring accordance with findability, accessibility, interoperability, and reusability (FAIR) principles.

The DCC has developed a robust data management platform based on Synapse, a data management platform that was developed by Sage Bionetworks. The platform is closely connected with NCI's Cancer Genomics Cloud. Dr. Cerami explained that data are transferred from the research centers to a central repository. Data from the research centers must adhere to a set of defined data standards. The data then are distributed to the research community through the dedicated HTAN Data Portal. Visualization options are provided through open-source software tools. Additionally, portions of data are transferred to different nodes within the CRDC. Dr. Cerami emphasized that HTAN data are part of the larger NCI cancer data ecosystem.

Data standards and integration have been developed within HTAN through a three-step process that involves community-driven requests for comments (RFCs), a unified schema providing validation and provenance, and support for different data levels. Dr. Cerami emphasized that numerous data types are supported (e.g., single-cell RNA sequencing, multiplex imaging), and several RFCs are in progress. Dr. Cerami briefly highlighted examples of data levels for different data types. The DCC supports five modes of data access: the HTAN Data Portal, visualization and exploratory analysis tools, Synapse, CRDC, and Google BigQuery. Dr. Cerami explained that different types of data can be found through the various modes. HTAN also maintains a strong collaboration with the Image Data Commons (IDC), and HTAN data will be available through the IDC in the future. Dr. Cerami demonstrated the data portal navigation and presented examples of data visualization using various tools.

Vanderbilt Pre-cancer Atlas HTAN Center: Biology Underlying the Initiation of Colorectal Cancer within a Diverse Population. Dr. Martha J. Shrubsole, Research Professor of Medicine, Vanderbilt University Medical Center (VUMC), presented an overview of the VUMC Pre-Cancer Atlas (PCA). She stated that current needs in the area of colorectal cancer include improved modalities for screening, as well as opportunities for prevention and interception. A better understanding of the molecular phenotypes of precancerous lesions, as well as of their progression and progression potential, is needed. The Colorectal Molecular Atlas Project (COLON MAP) is focused on mapping spatial and temporal relationships across the spectrum of the normal colon, early polyps, advanced polyps, and adenocarcinomas. Project participants are individuals who are scheduled for colonoscopies at VUMC. Because the participant pool is small, stratified sampling is employed to optimize the racial and ethnic diversity of the participants. Polyps are collected and bisected during standard-of-care colonoscopy; the first portion is allocated for clinical diagnosis, and the second portion is retained for research. Dr. Shrubsole emphasized that a standardized research pathology re-review of all polyps that are removed from every individual is crucial to this effort.

Dr. Shrubsole summarized the bottom-up model for colorectal tumorigenesis in which alterations within the stem cell compartment eventually lead to polyps and cancer. She explained that researchers have considered other models for tumorigenesis, similar to models of stomach tumorigenesis. The group's key questions were focused on finding evidence of a different origin of tumorigenesis, as well as understanding the tumor immune tone and microenvironment. Using RNA sequencing, Dr. Shrubsole's group identified different categories of transcriptionally abnormal epithelial cells. They found that adenoma-specific cells and serrated-specific cells exhibit different pathway profiles. Serrated-specific cells activate gene networks related to damage response and metaplasia.

Based on these findings, the group hypothesized that two different models of tumorigenesis exist: a classic bottom-up model and a top-down model involving differentiated cells. They mapped the location of neoplastic cells by multiplex immunofluorescence, as well as other histological imaging and single-cell RNA sequencing. Their findings suggested different cells of origin for the polyps. Additionally, microsatellite instable–high cancers retain the metaplastic signatures of serrated polyps, regaining some stem cell–like properties while retaining their own unique features. Additionally, MUC5AC expression appears to correlate with an absence or decrease of stem cell expression. The group also examined immune tone and found that cytotoxic immune cells were increased in serrated polyps in comparison to adenomas. To validate their findings functionally, the group partnered with the VUMC Gastrointestinal Specialized Program of Research Excellence (SPORE) to examine the question using mouse models and organoids. Dr. Shrubsole emphasized that her group's findings will fundamentally change how researchers consider carcinogenesis in the colon and will enable the research community to pursue different avenues to further study the polyps.

Trans-network projects (TNPs) are crucial to the HTAN. Dr. Shrubsole explained that her group has participated in multiple efforts to encourage collaboration across the HTAN centers. First, the SARDANA project is examining imaging methodologies across centers. The VUMC Cooperative Human Tissue Network Western Division provided samples for this effort. The Colorectal Liver Metastasis Project also provides an opportunity to cross-test platforms and methods and examine biological insights. The Tissue Cellular Neighborhoods Initiative was established to develop a gold standard set of cellular neighborhood annotations across tissues that can be used by the broader research community. Furthermore, the HTAN Diversity and Inclusion Working Group is developing an opportunity to include research advocates within the HTAN steering committee. The Working Group also is examining ways to address scientific questions related to diversity across the HTAN. Last, a newly established TNP is examining the effects of biofilms in colorectal carcinogenesis.

In summary, the group's contributions include a recruitment plan to optimize diversity, extensive characterization of participants and biospecimens, generation of a large single-cell RNA sequencing data set, deposition of data and publications, creation of open-source tools, leadership in multiple HTAN working groups, initiation of collaboration in multiple TNPs, training and research opportunities for junior investigators, and leveraging of other resources. Next steps include expanding sample size, adding additional imaging methodologies, developing methods for data analysis, following up on participant outcomes, publishing a newsletter and lay summaries, applying for additional funding, and exploring spatial transcriptomics.

OHSU Advanced Cancer Atlas HTAN Center: Dynamics of Tumor Evolution and Clinical Implications. Dr. Joe W. Gray, Professor Emeritus, Department of Biomedical Engineering, Oregon Health & Science University (OHSU), presented an overview of the OHSU Advanced Cancer HTAN Center. He explained that the Center is focused primarily on the dynamics of tumor evolution and clinical applications of evolutionary principles. The overarching goal of the Center is to identify tumor intrinsic and extrinsic mechanisms of response and resistance to therapy as they evolve across the patient and over time, with an emphasis on developing actionable guidance to address therapeutic resistance. His team is deploying diverse -omic and multiscale, multiplex imaging tools to identify mechanisms as they occur in

clinical real time. They are collecting detailed clinical data (e.g., blood biomarkers, anatomic images, dose–time treatment information) to help manage treatment. They have developed an infrastructure to collect and manage serial biospecimens, as well as the associated clinical and research information to interpret mechanisms as they arise. The Center also is involved in data sharing and collaboration, particularly in the areas of assay validation, data interpretation, and data integration.

Dr. Joe Gray outlined the Center's workflow, which involves acquiring serial biopsies and clinical information, obtaining patient consent, deploying validated -omic and imaging analysis tools to identify intrinsic and extrinsic mechanisms of resistance, and organizing integrated results for discovery research and clinical action. The team is obtaining serial biopsies and quickly preparing the specimens for spatial analysis. The process yields 11 analytical metrics for each patient. He emphasized the importance of collecting as much clinical information as possible within this workflow. He explained that the process has been automated, with most relevant information being extracted automatically from electronic health records. Clinical data elements and Clinical Laboratory Improvement Amendments (CLIA) assay results can be combined in a clinical data system to inform patient management.

From an -omics perspective, the goals of this effort are to identify mechanisms through comparative analysis of RNA sequencing data, DNA sequencing data, and reverse phase protein array data. Comparisons include pre versus on-treatment; patient versus the Serial Measurements of Molecular and Architectural Responses to Therapy (commonly called SMMART®) cohort and The Cancer Genome Atlas (TCGA). Features associated with response in preclinical data sets were identified, with an emphasis on identifying actionable mechanisms. Multiple metrics are quantified for each analysis, with a focus on intrinsic and extrinsic mechanisms. Reflex testing is performed when needed, using CLIA-approved assays so that the information can be used for patient management.

The team employs multiscale, multiplex tissue imaging, with a focus on assay development, development of metadata standards, and comparison to other modalities. They are focused on cell segmentation and proximity analysis, image management, and development of data dictionaries. Electron microscopy is used to elucidate ultrastructural features of cancers, and actionability is emphasized. Dr. Joe Gray explained that this process generates multiple types of data, which is managed using a robust data management system. The data can be managed, visualized, and exported to the DCC for distribution. The group is capturing data about the progression of responses to treatment.

Dr. Joe Gray explained that from a clinical perspective, this process yields detailed information about treatment, such as interactions and responses. From a genomics perspective, this process yields insight on how the tumors evolve under treatment. Researchers can identify clinically relevant mutations that provide insight on tumor evolution. Transcriptomic and proteomic analyses can provide additional information on these dynamics. Insights related to the immune response also are observed. With regard to the tumor microenvironment, the team has observed the importance of tumor "nests" that reflect stromal, cellular, and extracellular matrix boundaries. Additionally, 3D electron microscopy data can provide information relevant to receptor recycling, cell movement through tissue, drug sequestration, and nutrient scavenging.

The team now is working to move from single patients to larger cohort studies and on defining assay requirements and reducing the workflow size where possible. They also are interested in generating integrated multimodal and spatial biomarkers of response and resistance that can be tested in larger clinical trials, as well as in connecting with systems biology to elucidate functions and identify synergistic treatments. Additionally, the group is interested in exploring alternatives to invasive biopsies.

Questions and Answers

Dr. Barker asked whether the research community should begin compiling data to consider tumors in the context of evolutionary fitness landscapes. Dr. Joe Gray agreed and noted that the systems

biology community is beginning to recognize the importance of spatial data in understanding complex interactions.

Dr. Trey Ideker, Professor, Department of Medicine, University of California, San Diego, inquired about HTAN's intended scope. Dr. Joe Gray commented that these efforts generate numerous views of cancer (e.g., molecular networks, ultrastructure) that can be integrated. He noted the importance of considering one type of cancer in such integration efforts. NCAB Chair Dr. Carpten added that numerous biological factors contribute to the tumor microenvironment.

Dr. Chandrakanth Are, Jerald L. and Carolyn J. Varner Professor in Surgical Oncology and Global Health, Associate Dean for Graduate Medical Education, University of Nebraska Medical Center, inquired about security for atlases containing sensitive information, as well as access to the atlases.

Dr. Michael Becich, Chairman and Distinguished University Professor, Department of Biomedical Informatics, Professor of Pathology, Computing/Information, Clinical/Translational Sciences, and Bioengineering, Associate Vice Chancellor for Informatics in the Health Sciences, Co-Director, Center for Commercial Application (CCA) of Healthcare Data, Associate Director, Hillman Cancer Institute (HCI), Associate Director, Clinical and Translational Science Institute (CTSI), University of Pittsburgh School of Medicine, asked about integration with the Division of Cancer Biology (DCB)-supported Cancer Systems Biology Consortium (CSBC) and disease-focused SPOREs. Dr. Joe Gray responded that many of the HTAN Centers are connecting with SPOREs, as well as with various clinical programs within the systems biology community. Dr. Shrubsole added that many individuals within her Center are involved in other relevant activities, and joint efforts in this area have been established.

In response to a question from Dr. Becich about the sustainability of data sharing efforts, Dr. Cerami replied that HTAN's long-term goal for data involves storage through the CRDC. He is engaged in further conversations on this topic.

VII. ADJOURNMENT OF OPEN SESSION—DRS. JOHN D. CARPTEN AND KEITH T. FLAHERTY

Dr. Carpten adjourned the open session. Only NCAB members and designated NCI staff remained for the closed session.

VIII. NATIONAL CANCER ADVISORY BOARD (NCAB) CLOSED SESSION—DR. JOHN D. CARPTEN

"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.

The NCAB **en bloc** motion to concur with IRG recommendations was unanimously approved. During the closed session, a total of 2,612 NCI applications were reviewed requesting direct cost support of $ 1,070,981,771 and five FDA applications requesting direct cost support of $617,796.

IX. ADJOURNMENT OF CLOSED SESSION—DR. JOHN D. CARPTEN

Dr. Carpten adjourned the closed session at 5:29 p.m.

WEDNESDAY, 15 JUNE 2022

X. CALL TO ORDER AND OPENING REMARKS—DRS. JOHN D. CARPTEN AND KEITH T. FLAHERTY

Dr. Flaherty called Members to order on the final day of the 6th Virtual Joint Board Meeting of the BSA and NCAB and welcomed members of the Board, *ex officio* members, PCP members, liaison representatives, staff, and guests.

XI. RFA/COOP. AGR., AND PAR CONCEPTS—NEW—NCI PROGRAM STAFF

Division of Cancer Biology

The Metastasis Research Network (MetNet): MetNet Research Projects (U01) (New PAR)—Dr. Joanna Watson

Dr. Joanna Watson, Chief, Tumor Metastasis Branch (TMB), DCB, NCI, presented a new PAR concept to establish MetNet research projects, which was developed in collaboration with the MetNet programmatic team. Dr. Watson explained that MetNet was established in 2021 to incentivize collaborative, multidisciplinary basic research to expand mechanistic understanding of metastasis. This Network of U54 Metastasis Research Centers encourages use of systems-level approaches across chronological time and biological scales to consider the emergent processes required for tumor cell dissemination, colonization and growth, and treatment resistance. Each center is required to address two research themes that span the metastasis continuum from early dissemination to interaction and crosstalk, to dormancy (i.e., effects response, resistance to treatment, patient outcomes), and responses to therapy. Each center participates in monthly steering committee meetings and utilizes two working groups: the Resource and Data Sharing Group and the Patient Advocacy Group.

Four MetNet magnet centers were funded in the initial RFA and are integrated across shared organ or tissue biology, processes or systems, and research themes. In terms of scope, all four magnet centers explore interactions and crosstalk within the tumor microenvironment. Three of the four centers investigate how metastatic cells respond to different standard-of-care therapies to explore early dissemination of either breast or colorectal cancer cells. Only one center marginally addresses dormancy.

To address this research gap, the NCI is aiming to advance critical scientific opportunities in metastasis that could strengthen the MetNet. Regarding biology and systems, examples of opportunities include mechanisms of early dissemination for additional primary cancer sites (e.g., pancreatic, prostate, lung, kidney, bladder, or ovarian); those associated with distribution of distant metastases to certain organs; and those associated with sequential metastases. Other opportunities in this category include studies on the contribution of neural signaling networks and the influence of the macroenvironment and host physiology. Examples of opportunities to address dormancy include studies on the mechanisms associated with metastasis of cancer subtypes to multiple organs with different latencies and those associated with maintaining or releasing the related cancer from dormancy.

The NCI is proposing to add U01 research projects to build MetNet strategically. These projects aim to capitalize on the momentum and interest of using this approach, as evidenced by the initial RFA, and encourage systems-level approaches in areas underrepresented (e.g., dormancy) within the NCI research portfolio. A portfolio analysis of metastasis research revealed that 3 percent of DCB TMB research and 6 percent of NCI competing grant applications focus on dormancy. Five percent of the DCB TMB portfolio addresses systems approaches or systemic effects of cancer, most of which can be attributed to the CSBC. This PAR will be responsive to applicants who apply systems-level approaches to address one of the original MetNet FOA themes, designate a resource and data manager and an administrative manager, and allow set-aside funds (i.e., $25,000) for pilot projects in the later years of the project. Applications will be solicited in two receipt dates per year over 3 years and this PAR has no specific set-aside funds. The NCI anticipates funding 2 to 3 applications in each award cycle.

Subcommittee Review. Dr. Mary C. Beckerle, Chief Executive Officer, Huntsman Cancer Institute, Jon M. Huntsman Presidential Endowed Chair, Distinguished Professor of Biology and Oncological Sciences, Associate Vice President of Cancer Affairs, The University of Utah, expressed the Subcommittee's strong support for the concept. Dr. Beckerle conveyed that the Subcommittee recognizes that MetNet is a new NCI program and that it would be too early for a comprehensive evaluation. Dr. Beckerle commented on the strong scientific rationale to expand this research, given the critical importance of metastatic disease in forecasting poor patient outcomes. She continued that the strong interest from the scientific community of this research was evident in the response to the initial RFA, suggesting a pool of meritorious projects and a demand for research funding is this area. The Subcommittee appreciated the NCI staff responses to its requests for clarifications on the importance of including dormancy and its suggestions to expand the scope to include additional cancers contributing to the rising mortality rates.

Questions and Answers

Dr. Ashani T. Weeraratna, Bloomberg Distinguished Professor of Cancer Biology, E.V. McCollum Chair of Biochemistry and Molecular Biology, Johns Hopkins Bloomberg School of Public Health, Co-Program Leader, Cancer Invasion and Metastasis Sidney Kimmel Cancer Center, Johns Hopkins School of Medicine, lauded the NCI for proposing this critically important area of research and for offering robust awards, providing much-needed incentives.

Dr. Dubonei asked what the dissemination component was intended to accomplish in terms of overall outcomes of the program. Dr. Watson replied that the U01 funding mechanism requires a designated resource and data sharing manager for synchronization of the types of data to be shared across the network in the absence of a network coordinating center that normally performs this function.

Motion. A motion to approve the DCB's new PAR entitled "The Metastasis Research Network (MetNet): MetNet Research Projects" was approved unanimously**.**

Basic/Translational Research on Health Disparities in HIV/AIDS and Cancer (New RFA)— Dr. Elizabeth Read-Connole

Dr. Elizabeth Read-Connole, Head, Cancer Etiology Section, DCB, NCI, presented a new RFA concept for basic and translational research on health disparities in HIV/AIDS and cancer. The purpose of this RFA is to focus on the biological interactions of cancer health disparities in marginalized populations with an underlying HIV/AIDS infection. The NCI aims to address these cancer health disparities through basic mechanistic or translational studies to investigate how HIV interacts with the disparities to promote both non-AIDS-defining and AIDS-defining cancer initiation and progression, as well as the resulting pathogenic disease sequelae.

The U.S. HIV epidemic is marked by profound disparities between regions, stratified by race and ethnicity. These disparities have a disproportionate impact on marginalized populations, such as Black/African American and Latinx communities, women of color, people who inject drugs, men who have sex with men, and transgender persons. Persons with both cancer and HIV are frequently present in certain racial and ethnic populations, low socioeconomic groups, people living in geographically isolated areas, and people with limited access to proven screening tests, with higher rates of advanced cancer diagnosis. These effects are driven partially by a combination of health care provider shortages, low health literacy, and stigma. The most prevalent cancer types in the U.S. population among persons living with HIV are non-Hodgkin's lymphoma, Kaposi sarcoma (KS), and anal and lung cancers. This RFA was endorsed by the BSA *ad hoc* Subcommittee on HIV and AIDS Malignancy.

Dr. Read-Connole called attention to the potential biological differences in disease without an underlying HIV infection. For example, a 2020 study reported on the examination of gynecologic cytology case files for Black/African American and White/Caucasian women between 2017 and 2019. The results showed elevated rates of high-grade lesions, including carcinoma in African American women. A 2016 study on the immune profiles of Europeans and Africans in response to bacterial and viral infection found strong differences that predominantly affect antiviral and inflammation-related genes, with marked variances in responsiveness between Africans and Europeans. In terms of the U.S. rates of KS mortality by race and geographic region from 2000 to 2013, the hazard ratio for African Americans was significantly higher than that of White Americans. The survival rate in the United States is lower for African Americans living in the South. A portfolio analysis of health disparities, HIV/AIDS, and cancer revealed six grants funded by the NCI from 2018 to 2020. Projects related to Ending the HIV Epidemic in the U.S. currently funded by other NIH Institutes and Centers—including NIAID, the National Institute of Mental Health, and National Institute on Drug Abuse (NIDA)—address some aspects of health disparities in HIV, but do not address cancer.

To address the paucity of applications in this area of research, the NCI proposes this RFA to support studies investigating how health disparities interact with HIV to cause cancer. Other proposed research includes investigations of the role of oncogenic viral co-infections (e.g., KS-associated herpes virus) on cancer development, treatment, and outcomes in the aforementioned populations. Dr. Read-Connole emphasized that a future concept being developed by the Center to Reduce Cancer Health Disparities (CRCHD) and NCI Office of HIV and AIDS Malignancy will address social determinants of health, which are not the focus of this RFA. This research was submitted to and approved by the NIH Office of AIDS Research for FY 2023 high-priority AIDS research.

Subcommittee Review. Dr. Gloria D. Coronado, Mitch Greenlick Endowed Scientist in Health Disparities Research, Kaiser Permanente Center for Health Research, expressed the Subcommittee's support for the concept, which focuses on basic mechanistic and translational research. Dr. Coronado noted that the Subcommittee emphasized the need to include studies on health disparities among patients who are positive for HIV in this RFA. The Subcommittee appreciated the NCI staff responses to their suggestions on expanding the metric of success and clearly specifying the disparity.

The first-year cost for the one-time issuance is estimated at $4 M for seven to eight R01 awards and $1M for five-six R21 awards, with a total cost of $25 M for 5 years for R01s or 2 years for R21s.

Questions and Answers

Dr. Shelton Earp, Director, University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, Director, UNC Cancer Care, University of North Carolina at Chapel Hill, asked whether cohorts from sub-Saharan Africa or other areas where HIV is an epidemic would be included. Dr. Read-Connole explained that investigators who examine HIV and cancer have access to those data sets, collaborate in sub-Saharan Africa, and are welcome to apply for this initiative.

Motion. A motion to approve the DCB's new RFA entitled "Basic/Translational Research on Health Disparities in HIV/AIDS and Cancer" was approved unanimously.

Mechanistic Links Between Diet, Lipid Metabolism, and Tumor Growth Progression (New PAR)—Dr. Kristine Willis

Dr. Kristine Willis, Program Director, DCB, NCI, presented a new PAR to investigate the mechanistic links between diet, lipid metabolism, and tumor growth progression, which aligns with Goal 4 of the *2020–2030 Strategic Plan for NIH Nutrition Research*. Dr. Willis pointed out that cancer metabolism is a function of three interconnected components: tumor biology, tumor microenvironment, and nutrient availability; the latter is the focus of this concept. Research has shown that nutrients required for tumor growth and progression can originate from a variety of sources. These include the plasma, tumor interstitial fluid, stromal cells (e.g., cancer-associated fibroblasts, adipocytes), extracellular matrix, and diet. Recent studies suggest that diet-responsive lipid metabolism plays a central role in controlling tumor growth and progression. This emerging area of research provides the NCI a unique opportunity to support the advancement of fundamental cancer biology; recent discoveries have been timely and significant. Models that begin to incorporate the tumor microenvironment exist. Methodological innovations in the areas of metabolomics and lipidomics, computational and mathematical models, and systems biology approaches are more common. Despite these recent advances, challenges remain regarding biological complexity, quantitation of dietary variables, and insufficient bridges between research on nutrition and fundamental cancer biology. The NCI anticipates that this proposed concept will help address all of these challenges.

A portfolio analysis revealed that fundamental investigations of dietary influences on lipid metabolism are poorly represented in NCI research. In fact, previous initiatives related to diet and nutrition have focused primarily on cancer prevention, behavioral science, and the microbiome. Most NCI awards that study diet focus on epidemiology, risk and prevention, and the microbiome. From FY 2017 to FY 2021, the NCI made 15 awards from 113 competing grant applications that incorporated diet into mechanistic studies of one or more aspects of lipid metabolism.

This proposed concept would consist of two PARs using the R01 (5-year projects) and the R21 (2-year projects) mechanisms. The R01 grants under this program will aim to achieve three purposes: (1) support fundamental studies that identify and define molecular mechanisms through which diet modulates tumor growth and progression through lipid metabolism, (2) bridge the historically divided fields of nutrition and molecular metabolism, and (3) stimulate research and tool development in this emerging area. This concept also would fill gaps identified by subject-matter experts during the July 2021 DCB-hosted workshop on diet as a modifier of tumor metabolism. These include establishing and developing a community of practice composed of fundamental cancer biologists and nutritionists serving as multiple or co–principal investigators, and improving nutritional recommendations for patients, as well as the potential development of metabolic therapies.

Dr. Willis noted examples of research topics that would be responsive to this concept, including studies that address questions on the molecular mechanisms that moderate the differential effects of different biochemical species on dietary lipid on tumor progression and the influence of known cancer driver mutations (e.g., p53, KRAS) on lipid metabolism in tumor cells in response to diet. Applications that examine how the research topics contribute to health disparities are welcomed and encouraged. The evaluation of awards will be based on measurable performance criteria, including a change in the number of collaborations between nutrition scientists and researchers, the timely dissemination of research findings, and development of novel models and resources, as well as the sharing of those resources.

Subcommittee Review. Dr. Karen M. Basen-Engquist, Professor, Department of Behavioral Science, Division of Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, expressed the Subcommittee's enthusiasm and support for the concept, which is

addressing an important and timely topic aimed to attract robust attention in the field. Dr. Basen-Engquist suggested that patients with cancer are interested in answers to questions on diet and tumor progression and noted that this concept will help to build this evidence. The Subcommittee recognizes that this topic is underfunded in the NCI portfolio. Strengths of this concept highlighted include using the R01 and R21 mechanisms of the NCI Research Project Grant (RPG) pool, having nutritional scientists on the research team, and establishing a community of practice. The Subcommittee emphasized expanding the focus to include obesity and inflammation.

Questions and Answers

Dr. Leslie L. Robison, ALSAC Endowed Chair in Epidemiology, Chair, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Associate Director, St. Jude Comprehensive Cancer Center, asked whether applications focusing on cancer survivors would be included, given that dietary issues heavily impact this population. Dr. Willis responded that applications addressing tumor growth or exit from dormancy would be considered**,** as well as those focusing on obesity, the microbiome, and inflammation and lipid metabolism.

Dr. Sylvia Katina Plevritis, Chair and Professor of Biomedical Data Science, Professor of Radiology**,** Director, Biomedical Informatics Graduate Program, Stanford University School of Medicine, suggested including investigations to determine if diet is a function of the medications taken.

Dr. Andrew T. Chan, Chief, Clinical and Translational Epidemiology Unit, Massachusetts General Hospital (MGH), Director of Epidemiology, MGH Cancer Center, Daniel K. Podolsky Professor of Medicine, Harvard Medical School, sought clarity in the emphasis on fundamental science, but prioritizing multiple principal investigator applications from nutritionists, who can be registered dieticians or clinicians. Dr. Willis clarified that this concept is a fundamental molecular metabolism initiative that incorporates advice from nutrition scientists, nutritionists, and dieticians.

Dr. Fingert, Consultant, suggested including other types of specialists, such as immunologists and nuclear medicine experts. He called attention to the lung cancer treatment Alimta®, which is effective, has been shown to mitigate the toxicities to normal tissue, and has been patented as such. This treatment is endorsed in the nuclear medicine industry.

Motion. A motion to approve the DCB's new PAR entitled "Mechanistic Links Between Diet, Lipid Metabolism, and Tumor Growth and Progression" was approved unanimously.

Division of Cancer Control and Population Sciences

Advancing Adolescent Tobacco Cessation Intervention Research (New RFA)— Dr. Rachel Grana Mayne

Dr. Rachel Grana Mayne, Program Director, Division of Cancer Control and Population Sciences (DCCPS), NCI, presented a new RFA concept on advancing adolescent tobacco cessation intervention research. Dr. Grana Mayne explained that most tobacco use begins in adolescence, escalating in the mid to the late adolescent period in the high school years and the few years beyond. Research has shown that those who quit tobacco use can substantially avoid the risk of tobacco-caused morbidity and mortality, but adolescent tobacco use has become increasingly complicated in recent years. Greater tobacco product diversity exists and encompasses electronic nicotine delivery systems (ENDS), electronic (e) cigarettes, and cigar products (e.g., little cigars, cigarillos). ENDS and e-cigarettes often come in flavors and marketing that appeal to youth. This product diversity has engendered more complex use patterns, such as dual product use and co-use of cannabis and tobacco.

According to data from the 2020 National Youth Tobacco Survey, the current tobacco product use (i.e., in the past 30 days) among high school students is unacceptably high at nearly 24 percent for any tobacco products, with ENDS driving much of this use. The overall use rate of two or more products (i.e., dual use) is 8.2 percent of high school students. In terms of sociodemographic subgroups, cigar use is much higher among Black/African American youth at 9.2 percent, compared with White youth at 4.2 percent. Conversely, ENDS use is higher among Hispanic and White youth, compared with African American youth. These data underscore the need for the NCI to address all tobacco products in its tobacco cessation efforts to ensure no subgroup of adolescents is left behind and to advance health equity within these efforts.

Adolescence is a time when individuals are at the highest risk of the initiation, escalation, and entrenchment of tobacco use. Adolescent tobacco use develops along various trajectories with substantial heterogeneity in patterns of daily use to lower levels of intermittent use. Intervening during the adolescent years provides unique opportunities to disrupt this escalation of use early or treat established dependence. Because adolescence is a period of neurocognitive and psychosocial development, with an intense focus on establishing peer relationships, prefrontal cortex development, and self-regulatory skills development, adult cessation approaches will not be applicable.

Dr. Grana Mayne highlighted the evidence base for adolescent cessation interventions. Two-thirds of adolescent tobacco users report wanting to quit and nearly two-thirds report trying to quit. Empirically validated tobacco cessation interventions focusing on adolescents are limited. Two systematic reviews of adolescent cessation literature have been conducted in recent years: a 2017 report by the Cochrane group and a 2020 review by the U.S. Preventive Services Task Force. These reviews evaluated behavioral interventions tested in adolescents and studies with adolescents that tested the effects of medications that are FDA-approved for adult tobacco cessation. The major findings revealed minimal support for the currently tested behavioral interventions, no support for medication interventions, no studies focusing on noncigarette tobacco products, and few studies in populations that experience greater tobacco use burden. Both reviews acknowledge that mobile health and other digital platforms may be promising modes of treatment delivery.

Over the past few years, the NCI and other federal partners, as well as the scientific community and clinical partners, have aligned on the research needs and the urgency of treating adolescent tobacco use. An analysis of the NIH-wide portfolio found limited active grants conducting this type of research and none at the NCI. To meet this critical need, the NCI is proposing this RFA. The goal is to stimulate research on the development and evaluation of tobacco cessation interventions for adolescents, with a focus on the mid to late adolescent period. The scope includes interventions to effectively treat established tobacco dependence or disrupt escalation of tobacco use and to address the broad range of tobacco products and use patterns.

This RFA will be responsive to research that improves the effectiveness of existing tobacco cessation interventions, designs and plans for dissemination and implementation, and considers the needs of and includes populations that experience a greater burden of tobacco product use. Dr. Grana Mayne noted examples of research questions, including what comprises an effective digital therapeutic intervention and how to better engage and effectively engage youth in subgroups who experience tobacco-related health disparities. The NCI is planning to solicit R01 applications to test efficacy and effectiveness of interventions and gather strong preliminary data. The R34 mechanism will be used strategically to allow clinical trial planning grant activities. The NIDA plans to join the NCI in supporting this RFA.

Subcommittee Review. Dr. Dorothy K. Hatsukami, Associate Director of Cancer Prevention and Control, Forster Family Chair in Cancer Prevention, Masonic Cancer Center, Professor, Department of Psychiatry and Behavioral Sciences, University of Minnesota, expressed the Subcommittee's strong support for the concept. Dr. Hatsukami remarked that preventing the escalation in tobacco use is a novel

and potentially effective target. The Subcommittee appreciated the NCI staff responses to their suggestions to focus on diverse populations, incorporate implementation science within the research proposals, and consider cognitive behavioral tools in pharmacotherapy that would be complementary to the goals of this concept.

The first-year cost for the one-time issuance is estimated at $3 M for Year 1 and $5 M for Year 2 for 10 R01 and R34 awards, with a total cost of $33.5 M for 5 years.

Questions and Answers

In response to a question from Dr. Becich on the role of the NIDA, Dr. Kevin Walton, Chief, Clinical Research Grants Branch, Division of Therapeutics and Medical Consequences, NIDA, NCI, replied that tobacco cessation is a high priority for the NIDA, especially youth cessation given the increased use of ENDS. Dr. Walton pointed out the intent to fund commendable applications, noting that the NIDA routinely uses the R34 mechanism.

Dr. Hayes emphasized ensuring that the RFA language states that racial and ethnic minority differences must be highlighted in the intervention research.

Dr. Coronado asked about the feasibility of including biomarkers for the evaluation of self-reported data and whether the NCI is encouraging outcomes related to the maintenance or the long-term effect of the intervention. Dr. Grana Mayne explained that the NCI is not encouraging the biochemical verification of quitting smoking and noted that the RFA can support the continued use of treatments or the maintenance of the effects in long-term follow-up.

Dr. Vadaparampil suggested encouraging researchers to consider partnering with community groups that have a broad reach for adolescents, with a focus on young people ages 14 to 20.

Motion. A motion to approve the DCCPS' new RFA entitled "Advancing Adolescent Tobacco Cessation Intervention Research" was approved unanimously.

Cannabis and Cannabinoid Use in Adult Cancer Patients During Treatment: Assessing Benefits and Harms (New RFA)—Dr. Andrew N. Freedman

Dr. Andrew N. Freedman, Chief, Clinical and Translational Epidemiology Branch, DCCPS, NCI, presented a new RFA on assessing benefits and harms of cannabis and cannabinoid use in adult cancer patients during treatment. This RFA was developed in collaboration with the NCI-wide Cannabis and Cancer Research Interest Group (CCRIG). The rapidly increasing availability and use of cannabis by cancer patients, the lack of available evidence on the harms and benefits during cancer treatment, and the challenges to mounting clinical trials due to federal regulatory issues all speak to the need for a rapid infusion of multiple studies addressing cannabis use.

The purpose of this RFA is to support observational research studies to assess the benefits and harms of cannabis and cannabinoid use among cancer patients in active treatment. The NCI anticipates that these studies would provide critical information required to design and conduct future clinical trials. Cannabis or cannabinoids is referring to the cannabis plant, any cannabis-derived products, tetrahydrocannabinol, cannabidiol-only products, prescription cannabinoids, or any other products made with or derived from cannabis.

To better understand the state of cannabis in cancer research, the CCRIG hosted a 4-day conference in December 2020 on the topic and published a report in December 2021 in the *Journal of the National Cancer Institute Monographs* devoted to this symposium. Dr. Freedman noted that this symposium revealed that the legal landscape of medical and nonmedical cannabis use has changed

dramatically over the past decade, with wide variations in state policies. As of May 2022, 37 states and Washington, D.C., have legalized cannabis for medical conditions. Of these, 19 states and Washington, D.C., also have legalized the adult use of cannabis for recreation. The available delivery methods of these cannabis products also have undergone substantial changes and include oral, inhaled, and topical forms.

Patients with cancer use cannabis during treatment to manage such symptoms as anxiety, loss of appetite, nausea, pain, and sleep disturbance. Evidence suggests beneficial effects of cannabis use in these patients. For example, a 2017 study showed that large percentages (24 percent) of cancer patients reported using cannabis for physical and neuropsychiatric symptoms, recreational purposes, and to treat their cancer. This means one in four patients with cancer was using cannabis during their treatment, a rate that likely is even higher today. The data on the potential harms are limited. Three recent small-scale observational studies consistently showed an association between cannabis use and poor outcomes in patients with advanced cancers who were treated with immunotherapy. Because of the increased use of both immunotherapy and cannabis in patients with cancer, a better understanding of the possible interactions between the two therapies is needed.

U.S. medical oncologists regularly engage in discussions about cannabis use with their patients, but few feel sufficiently informed to make recommendations. Patients often ask their oncologist a range of questions about cannabis regarding improving symptoms, helping to treat their cancer, safety, and availability. Two key knowledge gaps identified from the 2020 symposium include (1) how and why patients with cancer are currently using cannabis and (2) the benefits and harms of this use associated with cancer and its treatment, comorbidities, and other medications patients may be administered.

The NCI has not awarded grants investigating the harms or benefits of cannabis use in patients with cancer for at least 6 years, and the need to collect this information to inform clinical trials is urgent. With this RFA, the NCI is seeking to support well-designed prospective cohort studies of patients with cancer who have solid or hematologic tumors and are currently receiving treatment. Studies will compare those patients using cannabis to those not using these products. Several key research questions in terms of the adverse effects of cannabis, dosing regimens, concomitant medications, mitigating or enhancing such effects, and the biological effects during treatment will need to be addressed. The RFA will support four U01 grants and one U24 coordinating center over a period of 5 years. Dr. Freedman noted that the CCRIG recently published a NOSI focusing on basic mechanisms of cannabis and cannabinoid action, with a specific emphasis on cancer biology, interception, treatment, resistance, and cancer symptoms. This proposed RFA complements that notice.

Subcommittee Review. Dr. Coronado expressed the Subcommittee's strong enthusiasm and support for the concept. She commented on the evidence demonstrating the relatively high use of cannabis among patients undergoing active cancer treatment, with little to no data on the potential harms or benefits. Dr. Coronado conveyed that the Subcommittee agreed with the focus on observational studies, given that regulations and the categorization of cannabis do not allow the randomization of participants to a cannabis or a non-cannabis treatment arm. The Subcommittee pointed out that 80 percent of patients with cancer who have solid tumors require surgical intervention and noted the need to include these patients in the clinical trials. The Subcommittee also noted one of the fastest-rising training programs in medical schools is addiction medicine and associated fellowships for training, underscoring the critical need for this research.

The first-year cost for the one-time issuance is estimated at $4.1M for four U01 awards and one U24 award, with a total cost of $20.5M ($16.5M for the U01s and $4.0M for the U24).

Questions and Answers

Dr. Karen M. Mustian, Dean's Distinguished Endowed Professor of Oncology and Surgery, Departments of Surgery, Radiation Oncology, and Public Health Sciences, University of Rochester

School of Medicine and Dentistry, asked about investigating clinical trial–ready approaches that address regulatory barriers. Dr. Freedman noted primary issues related to receiving FDA IND approval, manufacturing products, and recruiting patients. Discussions are ongoing within the NCI and across the NIH, including with the NIDA and the National Center for Complementary and Integrative Health, to address these issues. This RFA is a first step in working toward a solution, and having the NCI engage the BSA and NCAB in facilitating this research and challenges will be valuable.

In response to a question from Dr. Friese, Dr. Freedman explained that the NCI awarded administrative supplements to 12 Cancer Centers. These Centers, in a cross-sectional study, have been collecting data on 1,000 patients with cancer, their use of cannabis, and patterns of use. These preliminary data have been incorporated into this concept and suggest that the prevalence rates are much higher than the initial observations; further analyses are in progress. The aim is to move beyond the cross-sectional to prospective cohort design, collecting data on the harms and benefits.

Dr. Ideker suggested coordinating and clarifying messages regarding adolescent smoking cessation and adult cannabis use, which Dr. Freedman agreed was appropriate.

Motion. A motion to approve the DCCPS' new RFA entitled "Cannabis and Cannabinoid Use in Adult Cancer Patients During Treatment: Assessing Benefits and Harms" was approved unanimously.

Division of Cancer Prevention

Cancer Screening Research Network (CSRN) to Evaluate Multi-Cancer Early Detection Assays for Clinical Utility in Cancer Screening (New RFA)—Dr. Philip E. Castle

Dr. Philip E. Castle, Director, Division of Cancer Prevention (DCP), NCI, presented a new RFA concept for establishing the CSRN to evaluate MCED assays for clinical utility in cancer screening. The concept was developed in collaboration with the MCED Trial Team. The need for a CSRN is driven by the vast number of companies entering the MCED field, at the rate of one per month across cancer types and targets. The purpose of this RFA is to develop the network infrastructure to efficiently conduct cancer screening clinical trials and other important screening studies. The initial effort is to conduct a feasibility study, the Vanguard study, in preparation for a large randomized controlled trial (RCT) to evaluate MCED technologies or assays for the purpose of cancer screening.

Dr. Castle noted that clinical evaluation of screening modalities is needed. Emerging technologies are being introduced for commercialization without systematic evaluation of their use in the process of cancer screening. Studies are needed to address challenges with using MCED assays for cancer screening. Regarding clinical evaluation of risk-based screening strategies, trials are needed to evaluate strategies aimed to refine risk stratification of imaging and to evaluate risk stratification for screening. In its approach to establishing such a network, the DCP developed the proposed CSRN in collaboration with DCCPS to address questions related to the cancer screening continuum of care (e.g., efficacy, effectiveness, best practices, adoption, adaptation) and implementation for each step in this continuum. The approach considers that cancer screening trials require health care providers other than oncologists, site investigators contribute scientifically to the design of the trial or trials, and that a contemporary communication strategy is necessary.

The CSRN objectives are to establish the infrastructure needed to implement screening RCTs and other studies of screening and management for prevention/interception, beginning with the Vanguard study; conduct cancer screening trials to evaluate emerging technologies for cancer screening; and conduct cancer screening studies to evaluate other aspects of cancer screening, including clinical workflow and coordination of care. The CSRN will utilize the NCI Clinical Trials Enterprise System and will consist of one U01 coordinating and communication center, one UG1 data management and statistical center, and 10 to 15 UG1 Accrual, Enrollment and Screening Sites (ACCESS). Regarding the

ACCESS institutions, the NCI is seeking investigators with expertise in cancer screening and a history of recruiting participants into screening and prevention clinical trials and studies. The RFA will be responsive to institutions with demonstrated accrual and retention of participants on disease screening clinical trials, especially cancer screening or prevention and across a variety of health care settings (e.g., academic, community, health care systems). Applicants should have a demonstrated history of recruiting underserved populations.

A portfolio analysis of the Cancer Prevention and Control Clinical Trials Grant Program revealed clinical trials evaluating the operating characteristics of the cancer early detection technologies and communications, recruitment, and retention expertise, but no current studies of MCED technologies. The CSRN will complement the NCI Community Oncology Research Program (NCORP), the key DCP program that has been a successful network composed of oncology practices and investigators, but remains challenged to recruit participants to certain types of screening trials.

Dr. Castle provided some background information on MCED tests. Each MCED assay measures different analytes in the blood. Several markers (e.g., patterns of DNA methylation or fragmentation, RNA sequences, proteins) are being developed. Each MCED assay detects a different set of cancer types. A positive test result is a signal of cancer, but does not diagnose cancer. Some tests suggest a tissue of origin, and others require extensive imaging after a positive MCED result. Some companies developing MCED assays continue to refine their algorithms for determining a positive versus a negative result.

Unknowns about screening for cancer with MCED assays exist, such as whether screening a population of asymptomatic people for cancer with MCED assays will result in a mortality reduction from cancer. In addition, harms from using MCED assays to screen for cancer are unknown. The NCI hosted a study design workshop in October 2021, and staff provided the rationale and schema for a large RCT. The outcome was agreement among health care experts necessary to evaluate the MCED assays for clinical benefit. Aside from emphasizing the need for rigorously capturing and understanding the harms from MCED assays for cancer screening, workshop participants strongly supported a study to assess the feasibility of randomization and clinical workflow for the diagnostic pathway. On 21 January 2022, the NCI issued an RFI seeking input from developers of MCED assays on their readiness and willingness to participate in an NCI-sponsored clinical utility screening trial. The response period closed on 21 March 2022; 18 developers, 1 individual participant, and 17 companies responded. The NCI is in the process of meeting with the developers.

Dr. Castle described the first CSRN study, the Vanguard study. The schema for step-wise "go/no-go" validation includes minimum performance qualifications, reference set assessment, a feasibility study—which is, in this case, the Vanguard study—and an RCT. Study participants will be randomized to one of three arms: a control, which includes no additional tests; and two interventions, MCED 1 or MCED 2, with different cancer assessments. All arms will offer standard-of-care screenings. The objectives of Vanguard are to assess participant willingness to be randomized, determine adherence to testing and diagnostic follow-up, evaluate the feasibility of protocol-defined diagnostic workflows, determine the reliability and timeliness of blood specimen testing and return by the MCED companies, and identify facilitators and barriers to recruitment, retention, and compliance of a diverse participant group. The estimated sample size for the study is 8,000 participants per arm to have a 164 screen positive output to support reasonable confidence levels around diagnostic resolution.

The MCED RCT design is similar to Vanguard's, but with additional study arms and interventions and the inclusion of primary endpoints. The overarching goals of Vanguard is to assess feasibility and finalize RCT design logistics. The overall goal of the RCT is to assess benefits, harms, and generalizability of the MCED tests. Both studies are assay agnostic and employ a multi-arm platform design that allows dropping tests that do not perform well and adding new arms for promising new tests. Data sharing will follow FAIR principles. A biorepository will be established for validating new tests,

supporting natural history studies, and performing comprehensive characterization of tumors, potentially at molecular stages or states never before observed.

The NCI MCED Trial Team is composed of representatives from across the NIH, FDA, and CMS. Ongoing activities include coordinating key intramural–extramural working groups. These include the Assay Working Group, Diagnostic Pathway Working Group, Ethics and Equity Working Group, and Trial Design Working Group.

Subcommittee Review. Dr. Ideker expressed the Subcommittee's enthusiasm and support for the concept. He commented that the Subcommittee agreed that well-controlled studies are needed for MCED test screening, especially with the growing number of assays being developed, largely marketed as direct-to-consumer products. The Subcommittee is confident that this concept will establish the needed infrastructure and achieve its goals. Dr. Ideker pointed out that the program will consist of multiple components: the CSRN, the Vanguard study, and a large-scale MCED RCT. The Subcommittee emphasized not losing sight of the overall goal of the long-term potential to improve screening platforms and patient health; providing further details on the specific data types and diagnostic assays being sought for the study; collaborating with the FDA on the MCED screening tests; and thinking ahead about the complexity with alternative trials in progress in the private sector.

The first-year cost for the one-time issuance is estimated at $15.5 M for one U01 award for a coordination center, one UG1 award for a data management center, and 10 to 15 UG1 awards for ACCESS institutions, with a total cost of $73.5 M for 4 years.

Questions and Answers

Dr. Ian M. Thompson, Jr., President, CHRISTUS Santa Rosa Medical Center Hospital, Texas Urology Group, commented on his experience with prostate cancer and the early days of prostate-specific antigen (PSA) testing. He emphasized the importance of leveraging the expertise within the NCI clinical trials cooperative groups and their large prevention trials, such as the Prostate Cancer Prevention Trial (commonly called PCPT) and the Selenium and Vitamin E Cancer Prevention Trial (commonly called SELECT).

Dr. Brawley reflected on the PSA testing story and agreed with the need to engage the cooperative groups. He emphasized the importance of not creating disparities and recommended against primarily considering Federally Qualified Health Centers.

Dr. Margaret R. Spitz, Professor Emeritus, Department of Medicine, Dan L. Duncan Cancer Center, Baylor College of Medicine, asked about a systematic process to evaluate and select biomarkers in the study. Dr. Castle clarified that MCED tests, not biomarkers, were being assessed in these studies. The NCI is agnostic about any MCED test or panel, company, or technology. A four-stage process for testing is in development; the first stage has been completed, and data have been published. The reference set for evaluation is being established by the Alliance for Clinical Trials. Dr. Plevritis expressed interest in capturing sequencing data, in parallel, when they are collected.

Dr. Mustian commented on the history of the cooperative groups, NCORP, and NCI's National Clinical Trials Network (NCTN) as well as the infrastructure in efforts to bring cancer treatment clinical trials to patients in the community, which involved oncologists. She emphasized engaging these groups in the proposed CSRN.

Motion. A motion to approve the DCP's new RFA entitled "Cancer Screening Research Network (CSRN) to Evaluate Multi-Cancer Early Detection Assays for Clinical Utility in Cancer Screening" was approved unanimously.

Office of the Director

Transformative Educational Advancement and Mentoring Network (TEAM) (New RFA)—Dr. LeeAnn Bailey

Dr. LeeAnn Bailey, Chief, Integrated Networks Branch, CRCHD, NCI, presented a new RFA concept for establishing the TEAM. Dr. Baily highlighted that this concept is an activity of the Working Group 2 of the NCI Equity and Inclusion Program, overseen by the NCI Equity Council. Recent efforts by both the NCI and the NIH are providing opportunities to increase diversity in funded cancer investigators through programs such as the NCI Continuing Umbrella of Research Experiences (CURE) and the NCI Partnerships to Advance Cancer Health Equity (PACHE). Despite these efforts, a substantial gap in the representation of racial and ethnic minorities in the scientific enterprise and workforce continues. Targeted efforts are needed to ensure that cancer trainees and ESIs have the programmatic and institutional resources necessary. Outreach to minority-serving institutions (MSIs) to identify and assist with the development of underrepresented scholars might be beneficial.

Training navigation used by the NCI over the past 5 years has proved invaluable to helping scholars infuse into, progress in, and advance through the academic pipeline. Funding opportunities are vehicles to career independence but can be overwhelming to trainees in terms of selecting the optimal mechanism for which to apply, understanding how to prepare the application, and knowing how to respond to the peer-review process. The NCI recognizes that having a qualified expert to assist scholars focused on this process can be advantageous. One such program that has leveraged training navigation at the NCI is the Geographic Management of Cancer Health Disparities Program (GMaP). In FYs 2019 through 2020, GMaP and training navigation resulted in more successful applications to CURE—36 percent in 2019 and 45 percent in 2020, in comparison with the overall NIH success rate of 30 percent for both years. Localized navigation support at the institutional level is required to ensure that scholars at MSIs receive continuous personal training and coordination, education, and support.

The purpose of TEAM is to pilot the use of training champions at MSIs to provide educational and career development for underrepresented scholars. TEAM has three main objectives, to: (1) pilot the use of training champions; (2) leverage the training champions and the institutional support to connect a potential scholar group with mentoring and networking opportunities; and (3) adapt or leverage culturally tailored educational activities. The Network will provide multiple levels of support, including direct support for scholars by the training champions, who will help address the underrepresentation and attrition within the workforce pipeline; institutional support at MSIs from principal investigators, faculty, or mentors; and NCI technical assistance from the training navigation team.

The NCI envisions the training champion as one full-time equivalent, or a team contributing a time effort equaling one full-time equivalent, who would provide hands-on support to the scholars. These individuals can reside at the institution being served or be recruited from external positions. The training champions will have the full support of NCI program staff, receive formalized training, and be integrated into the training navigation team at CRCHD. Regarding networking, the team concept is centered on the scholar's individual growth. Long-term sustainability will require support that leverages resources and infrastructure at the institutional level and will be a key objective of the grant. This concept also encourages innovation. The NCI anticipates that the opportunity to adapt or leverage culturally tailored educational activities and short courses will enhance not only subject-matter expertise but also career development. TEAM promotes effective mentor–mentee communication strategies and trains scholars in ethics, implicit bias, microaggressions, and structural inequities. Potential applicants for this RFA are encouraged to engage in innovation laboratories, crowdsourcing, and network science to optimize the learning experience for scholars. The NCI is proposing the R25 mechanism to support five TEAM grantees. In closing, Dr. Bailey highlighted an example of successful training navigation of a scholar connected with GMaP who advanced through the NCI programs to achieve a K award.

Subcommittee Review. Dr. Suzanne J. Baker, Associate Director of Basic Sciences, St. Jude Comprehensive Cancer Center, Endowed Chair in Brain Tumor Research, St. Jude Children's Research Hospital, expressed the Subcommittee's enthusiasm and strong support for the concept. Dr. Baker commented on the concept's structure to engage scholars at different stages of their training and leverage existing NCI programs, noting that the earlier individuals can be engaged and mentored, the greater their chance of building a career path forward. The Subcommittee appreciated NCI staff responses to their questions on specific examples of frameworks to be addressed in the applications, who would be the training champion (e.g., well-funded investigator), and the overall scope of the program. In addition, the Subcommittee emphasized empowering a network-type approach in the early phase of the program.

The first-year cost for the one-time issuance is estimated at $2.55 M for five R25 awards, with a total cost of $12.75 M for 5 years.

Questions and Answers

Dr. Fingert commented on how mentoring grant recipients who are leading clinical trials could result in improvements in some modern therapies (e.g., stem cell therapies). He noted the success of group mentoring programs. Dr. Bailey explained that with TEAMS, the NCI is anticipating multiple trainees participating, engaging a cadre of training champions, and fostering collaborations across the MSIs and other academic centers, as well as the Cancer Centers.

Motion. A motion to approve the Office of the Director's (OD) new RFA entitled "Transformative Educational Advancement and Mentoring Network (TEAM)" was approved unanimously.

Cancer Moonshot Scholars Diversity Program (New RFA)—Dr. LeeAnn Bailey

Dr. Bailey presented a new RFA concept for establishing the Cancer Moonshot Scholars Diversity Program. A biomedical research workforce that capitalizes on the full spectrum of the nation's skills, talents, and viewpoints is essential for solving complex health problems, including cancer. The involvement of individuals with diverse cultural perspectives has been shown to be essential to reach diverse communities and make advancements in addressing cancer health disparities. The NCI, in alignment with the NIH and the White House, continues to demonstrate a strong commitment to attracting, training, and retaining the best minds from diverse backgrounds to ensure long-term successes in the cancer research enterprise. The White House's new Cancer Cabinet recently announced that one priority of the reignited Cancer Moonshot will be to inspire and support the next generation of diverse cancer researchers. This concept aims to promote scientific advances in cancer research through the diversification of the pool within the NCI R01 portfolio. This program will focus on ESIs from underrepresented groups to increase the number of funded R01 investigators from these groups across the cancer research continuum.

Individuals from underrepresented groups—including Black/African American, Hispanic/Latino, American Indian, Alaska Native, Native Hawaiian, and other Pacific Islanders—represent a growing segment of the U.S. population. However, these groups are disproportionately represented within the NCI R01 portfolio. The demographics of the FY 2020 NCI R01 and R01-equivalent applicants showed that in aggregate, the number of applicants from underrepresented groups was markedly less than from non-underrepresented groups, specifically non-Hispanic White/Caucasian and Asian applicants. This decrease in the number of applications from underrepresented groups (e.g., Black/African American) has led to lower representation in NCI's awardees in comparison to the overall applicant pool. Dr. Bailey pointed out that this funding gap, first identified in 2011 and further confirmed in the literature, is not specific to the NCI, but is a challenge for the NIH overall. Trends in the NCI R01 and R01-equivalent funding from FY 2010 to FY 2020 revealed a disparity between the Black/African American and the Hispanic/Latino underrepresented groups in comparison with their White/Caucasian and Asian counterparts. This concept aims to address these challenges.

Dr. Bailey explained that the eligibility criteria for the Cancer Moonshot Diversity Program will be consistent with the NIH Diversity Statement (NOT-OD-20-031). ESIs from underrepresented groups are especially encouraged to apply, and there are no restrictions on the type of cancer research to propose. The RFA will be responsive to applications proposing research topics spanning the entire cancer continuum. Multi–principal investigator applications are permissible, with the stipulation that an investigator from an underrepresented group must be designated as the contact principal investigator.

The program will be led by CRCHD with NCI-wide input and participation from the Divisions, Offices, and Centers across the NCI. The NCI-wide steering committee will review all R01 applications and ensure appropriate docket assignment depending on referral guidelines. The steering committee members will additionally contribute to outreach activities to ensure a broad range of applicants are made aware of the RFA. Cancer Moonshot funds are being requested to support this program. The NCI anticipates funding 15 new R01 awards per year for 3 years, supporting projects up to 5-years. Regarding metrics and evaluation criteria, the NCI expects that this program will increase the number of ESI applicants from underrepresented groups in the NCI R01 application pool, as well as the award pool. The program management will monitor the productivity of the funded R01 investigators, including the number and quality of their publications and scientific presentations and sessions. Dr. Bailey acknowledged the tireless efforts of CRCHD Director Dr. Sanya Springfield and the entire NCI leadership for being champions for diversity and for their contributions over the years.

Subcommittee Review. Dr. Brawley expressed the Subcommittee's enthusiasm and strong support for the concept, which is providing opportunities for underrepresented groups. The Subcommittee commended the NCI on this initiative, which is long overdue and suggested a sustainability plan to build the workforce pipeline beyond the 5 years.

The first-year cost for the three-time issuance is estimated at $9 M for 15 R01 awards, with a total cost of $135 M for 5 years.

Questions and Answers

Dr. W. Kimryn Rathmell, Hugh Jackson Morgan Professor of Medicine and Biochemistry, Chair, Department of Medicine, Physician-in-Chief, Vanderbilt University Medical Center, sought clarity on how the multiple principal investigator and designated contact principal investigator from an underrepresented group would work. Dr. Bailey clarified that the program is encouraging ownership among the principal investigators from underrepresented groups, with the benefits of having multiple principal investigators to increase the opportunities for success. Dr. Lowy added that multiple principal investigator awards currently account for one-third of the NCI's total funding. ESIs included on such a team have experienced increased difficulty securing an individual award. Having the ESI serve as the contact principal investigator is one way this program can help with future awards.

Dr. Melissa L. Bondy, Chair and Professor, Department of Epidemiology and Population Health, Co-Director, Center for Population Health Sciences, Associate Director for Population Sciences, Stanford Cancer Institute, expressed appreciation to the NCI for this program and to the Subcommittee for endorsing it. She highlighted the importance of having a forum to convene the scholars and promoting mentoring, including among peers, as a means to retaining investigators in the field. Dr. Bailey called attention to another NCI Equity and Inclusion Program initiative, the NCI Early Investigator Advancement Program (EAIP). The first EAIP cohort of 20 researchers just began and is engaged in mentoring/peer mentoring activities, with the goal of attaining a first R01.

Motion. A motion to approve the OD's new RFA entitled "Cancer Moonshot Scholars Diversity Program" was approved unanimously.

XII. PAR RE-ISSUE CONCEPTS—DR. PAULETTE S. GRAY

Dr. Paulette S. Gray, Director, DEA, presented nine 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. Paulette Gray reminded the BSA of the NIH policy established in 2019 that requires an open forum discussion and acceptance by an Advisory Council or Board for new and re-issue RFAs, RFPs, and PARs. Because of the large volume of PAR re-issues that the NCI receives annually, the BSA will review the re-issues as a group, not individually, and will vote to concur with the re-issuances.

- Feasibility Studies to Build Collaborative Partnerships in Cancer Research (P20 Clinical Trial Not Allowed) (PAR-18-91)
- Comprehensive Partnerships to Advance Cancer Health Equity (CPACHE) (Collaborative U54 Clinical Trial Optional) (PAR-18-767)
- Biology of Bladder Cancer (R01 Clinical Trial Optional); PAR-19-184: Biology of Bladder Cancer (R21 Clinical Trial Optional) (PAR-19-183)
- Co-infection and Cancer (R21 Clinical Trial Not Allowed) (PAR-20-061); Co-infection and Cancer (R01 Clinical Trial Not Allowed) (PAR-20-062)
- Bioengineering Research Grants (BRG) (R01 Clinical Trial Not Allowed) (PAR-19-158); Bioengineering Research Grants (BRG) (R01 Clinical Trial Required) (PAR-19-159)
- NCI Clinical and Translational Exploratory/Developmental Studies (R21 Clinical Trial Optional) (PAR-20-292)
- Revision Applications for Validation of Biomarker Assays Developed Through NIH-Supported Research Grants (R01 Clinical Trial Not Allowed) (PAR-20-074)
- NCI Small Grants Program for Cancer Research for Years 2020, 2021, and 2022 (NCI Omnibus R03 Clinical Trial Optional) (PAR-20-052)
- NCI Program Project Applications (P01 Clinical Trial Optional) (PAR-20-077)

Questions and Answers

In response to comments from Dr. Fingert about budgets, Dr. Paulette Gray clarified that PARs do not have set-aside dollars and noted that once the applications are received, the NCI leadership will ascertain or decide upon the budgets. Board members are encouraged to reach out to Dr. Gray with any further questions.

Motion. A motion to concur on the nine PAR re-issuances was approved unanimously.

XIII. ONGOING AND NEW BUSINESS—DRS. JOHN D. CARPTEN AND KEITH T. FLAHERTY

NCAB Planning and Budget Subcommittee. Dr. Barker, Chair of the NCAB Planning and Budget Subcommittee, presented the report of the 13 June 2022 meeting. The NCI Acting Director, Dr. Lowy, attended the meeting. Dr. Barker stated that the NCI has set a goal to achieve a payline of 15 percent by FY 2025; the current payline is 11 percent. Payline increases result in increased commitments for the next several fiscal years. The enacted budget for FY 2022 included an increase of 7.6 percent for the NIH and an increase of 5.4 percent for the NCI. These figures include $194 M for the Cancer Moonshot and $50 M for the Childhood Cancer Data Initiative. Dr. Barker also reminded the attendees that the initial Cancer Moonshot is in its final year; the reignited Cancer Moonshot could provide additional funding to the NCI. The NCI received its appropriations for FY 2022 in March, and the Administration built its FY 2023 budget proposal using the FY 2022 continuing resolution as the current year baseline. As a result, the President's proposed NCI budget for FY 2023 includes a cut of $199 M.

Dr. Barker remarked that the NCI has experienced an increase in funding applications, reflecting new cancer research opportunities. Additionally, the resources for the reignited Cancer Moonshot are unclear. Dr. Barker noted that the next phase of the Cancer Moonshot will reflect an all-of-government approach involving multiple federal agencies. She emphasized the importance of conveying that the NCI is well suited to serve as the headquarters for this effort. Dr. Barker added that ARPA-H has been approved, and the Subcommittee discussed funding for this effort. She noted that the positions of NIH Director, NCI Director, and ARPA-H Director are open, and much remains unknown. Dr. Barker underscored the important role of the advocacy community during uncertain times and commented that the NCI budget likely will be a focus of conversation on Capitol Hill in the near future.

Motion. A motion to accept the report of the 13 June 2022 NCAB Planning and Budget Subcommittee meeting was approved unanimously.

NCAB *Ad Hoc* Population Science, Epidemiology, and Disparities Subcommittee. Dr. Paskett Chair of the NCAB *ad hoc* Population Science, Epidemiology, and Disparities Subcommittee, presented the report of the 13 June 2022 meeting. The NCI Acting Director, Dr. Lowy, attended the meeting. Dr. Paskett reported that Subcommittee members were updated on the progress of the NCAB *ad hoc* Working Group on Strategic Approaches and Opportunities for Research on Cancer Among Racial and Ethnic Minorities and Underserved Populations (Working Group). Dr. Elena Martinez, Working Group Co-Chair, reviewed the charge, which is to identify and evaluate the current status of—and barriers to progress on—cancer research on racial and ethnic minorities and underserved populations. Working Group membership was confirmed in April 2021, and the first Working Group meeting took place in July 2021. The three Working group co-chairs (Drs. Paskett, Martinez, and Doubeni) meet monthly to set the agenda with Dr. Castle, the designated federal official and Working Group Executive Secretary. Monthly full committee meetings have featured speakers from the Center for Research Strategy (CRS), DCCPS, and CRCHD. A smaller portfolio analysis task group, led by Working Group member Dr. Chanita Hughes-Halbert, worked with the CRS team to operationalize a definition of health disparities and refine the NIH funding portfolio search criteria.

Dr. Paskett noted that the 13 June 2022 Subcommittee meeting minutes contain an outline of the Working Group's upcoming report. The CRS method for information gathering included a pilot strategy using search terms related to Black/African American. The pilot strategy was assessed before the refined methodology was applied and expanded to all relevant populations, which comprised Hispanic/Latino, American Indian or Alaska Native, Asian or Pacific Islander, rural, older adult, LGBTQ+, and adolescent and young adult (AYA) populations. The CRS team will report the results to the Working Group at the 22 June 2022 meeting.

The Subcommittee was briefed on emerging gaps and recommendations identified by the Working Group. Research focused on age-specific populations (e.g., AYA, older adult) could not be categorized and only a limited amount of data was collected for LGBTQ+ populations. These abilities must be refined and improved. The goal of the Subcommittee is to present these results at the 5–7 December 2022 Joint BSA and NCAB Meeting. Dr. Paskett thanked the Working Group, the co-chairs, and the CRS for their significant efforts.

Motion. A motion to accept the report of the 13 June 2022 NCAB *ad hoc* Population Science, Epidemiology, and Disparities Subcommittee meeting was approved unanimously.

Other Business. Dr. Barker suggested establishing an NCAB *ad hoc* Working Group to assess the consequences of using the readout (i.e., cancer signals) of MCED tests in clinical practice.

Future Agenda Items. The BSA and NCAB members suggested future presentations on the alignment of the scientific concepts (e.g., PARs, RFAs) with the NCI strategic plan, effects of high attrition of trainees in cancer research from universities into industry, impact of the NCI budget on career

growth and research, and a report on the status of ARPA-H. Members were asked to forward any additional suggestions for potential future agenda items to the respective Board chairs and Dr. Paulette Gray.

XIV. ADJOURNMENT—DRS. JOHN D. CARPTEN AND KEITH T. FLAHERTY

Dr. Carpten thanked all the Board members, as well as the visitors and observers, for attending. There being no further business, the 6th Virtual Joint Meeting of the BSA and NCAB was adjourned at 5:02 p.m. on Wednesday, 15 June 2022.

Date	Keith T. Flaherty, M.D., Chair, BSA
Date	John D. Carpten, Ph.D., Chair, NCAB
Date	Paulette S. Gray, Ph.D., Executive Secretary