

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

**5<sup>th</sup> VIRTUAL JOINT MEETING  
of the  
BOARD OF SCIENTIFIC ADVISORS AND  
NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting  
December 7–9, 2021**

**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  
7–9 December 2021**

The Board of Scientific Advisors (BSA) of the National Cancer Institute (NCI) and the National Cancer Advisory Board (NCAB) convened for the 5<sup>th</sup> Virtual Joint Meeting on 7–9 December 2021. The meeting was closed to the public on Tuesday, 7 December 2021, from 12:00 p.m. to 1:11 p.m., and open to the public on Wednesday, 8 December 2021, from 1:00 pm to 5:49 p.m., and Thursday, 9 December 2021, from 1:00 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, presided during the open session. Dr. Scott W. Hiebert, Hortense B. Ingram Chair in Cancer Research, Professor of Biochemistry, Department of Biochemistry, Vanderbilt University School of Medicine, 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. Chandraknath Are\*  
Dr. Suzanne J. Baker\*  
Dr. Karen M. Basen-Engquist  
Dr. Michael John Becich  
Dr. Mary C. Beckerle (absent)  
Dr. Melissa L. Bondy  
Dr. Otis W. Brawley  
Dr. Andrew T. Chan\*  
Dr. Nelson J. Chao  
Dr. Gloria D. Coronado  
Dr. Chyke A. Doubeni  
Dr. Shelton Earp  
Dr. Dorothy K. Hatsukami  
Dr. Trey Ideker\*  
Dr. Karen E. Knudsen  
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 (absent)  
Dr. David Sidransky  
Dr. Ian M. Thompson, Jr.  
Dr. David A. Tuveson  
Dr. Robert H. Vonderheide  
Dr. Richard C. Zellars\*

**NCAB Members**

Dr. John D. Carpten (Chair)  
Dr. Peter C. Adamson (absent)  
Dr. Francis Ali-Osman  
Dr. Nilofer S. Azad\*  
Dr. Anna D. Barker  
Dr. Deborah Watkins Bruner  
Dr. Yuan Chang (absent)  
Dr. Luis Alberto Diaz, Jr.\*  
Dr. Howard J. Fingert  
Dr. Christopher R. Friese\*  
Mr. Lawrence O. Gostin (absent)  
Dr. Andrea A. Hayes-Jordan  
Dr. Amy B. Heimberger\*  
Dr. Scott W. Hiebert  
Dr. Nikan Khatibi (absent)  
Dr. Timothy J. Ley  
Dr. Electra D. Paskett  
Dr. Nancy J. Raab-Traub  
Dr. Margaret R. Spitz  
Dr. Susan Thomas Vadaparampil  
Dr. Ashani T. Weeraratna\*  
Dr. Max S. Wicha  
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. Richard Pazdur, FDA (absent)
Dr. Joseph R. Graber, DOE	Dr. Craig D. Shriver, DoD
Dr. Michael Kelley, VA	Dr. Kerry Souza, NIOSH (absent)
Dr. Aubrey Miller, NIEHS	Dr. Lawrence A. Tabak, NIH (absent)

**Members, Scientific Program Leaders, National Cancer Institute, NIH**

Dr. Norman E. Sharpless, Director, National Cancer Institute  
Dr. L. Michelle Bennett, Director, Center for Research Strategy  
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. William Dahut, Scientific Director for Clinical Research, Center for Cancer Research  
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research  
Dr. Dan Gallahan, 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. Sara Hook, Associate Director, Strategic Scientific Partnerships  
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. Douglas R. Lowy, Principal Deputy Director, National Cancer Institute  
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research  
Dr. Tom Misteli, Director, Center for Cancer Research  
Dr. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program  
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 Bioinformatics 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  
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

**TABLE OF CONTENTS**

**TUESDAY, 7 DECEMBER 2021**

I. NCAB Closed Session—Dr. Scott W. Hiebert..... 1

**WEDNESDAY, 8 DECEMBER 2021**

II. Call to Order and Opening Remarks—Drs. John D. Carpten and Keith T. Flaherty..... 1

III. NCI Director’s Report—Dr. Norman E. Sharpless..... 1  
 Questions and Answers ..... 6

IV. Legislative Report—Ms. M.K. Holohan..... 6

V. Recognition of Retiring NCAB Members—Dr. Norman E. Sharpless ..... 7

VI. Cancer Moonshot<sup>SM</sup>: Looking Ahead—Dr. Dinah S. Singer..... 7  
 Questions and Answers ..... 10

VII. The NIH Common Fund: Faculty Institutional Recruitment for Sustainable Transformation  
 (FIRST) Program—Dr. Sanya A. Springfield ..... 10  
 Questions and Answers ..... 11

VIII. Challenges and Opportunities in Cancer Control and Population Sciences—  
 Dr. Robert T. Croyle..... 11  
 Questions and Answers ..... 14

IX. RFA/Coop. Agr., RFP, and PAR Concepts—New and Re-Issue—NCI Program Staff..... 14  
 Office of the Director  
 Global Implementation Science for Equitable Cancer Control (GlobalISE Cancer  
 Control) (New RFA/Coop. Agr.)—Dr. Gila Neta..... 14  
 Division of Cancer Prevention  
 PREVENT Cancer Preclinical Drug Development Program (Re-Issue RFP)—  
 Dr. Shizuko Sei ..... 15  
 Division of Cancer Control and Population Sciences  
 Cancer Epidemiology Cohorts: Research Opportunities in Established Studies (New PAR)—  
 Dr. Joanne Elena ..... 17  
 Cancer Epidemiology Cohorts: Building the Next Generation of Research Cohorts  
 (Clinical Trials Not Allowed) (New PAR)—Dr. Tram Kim Lam ..... 18  
 Cancer Control Research in Persistent Poverty Areas (New RFA/Coop. Agr.)—  
 Dr. Shoba Srinivasan..... 19

**THURSDAY, 9 DECEMBER 2021**

X. Call to Order and Opening Remarks—Drs. John D. Carpten and Keith T. Flaherty..... 20

XI. Division of Cancer Prevention: Vision—Dr. Philip E. Castle ..... 20  
 Questions and Answers ..... 22

XII. Achieving Health Equity through Prevention and Implementation Science of Patient  
 Navigation in Underserved Populations—Dr. Melissa A. Simon ..... 22  
 Questions and Answers ..... 24

XIII. Implementing Program-Based Interventions to Improve Population-level Lung Cancer  
 Outcomes: The Mid-South Miracle—Dr. Raymond U. Osarogiagbon ..... 24  
 Questions and Answers ..... 25

XIV. RFA/Coop. Agr. and PAR Concepts—New and Re-Issue—NCI Program Staff..... 25  
 Division of Cancer Treatment and Diagnosis/Division of Cancer Biology  
 Pediatric Immunotherapy Network (PIN) (New RFA/Coop. Agr.)—Dr. Anju Singh..... 25  
 Division of Cancer Biology/Office of the Director  
 Integrating Health Disparities into Immuno-Oncology Research (HDIO) (New RFA)—  
 Dr. Lillian Kuo ..... 27

	Division of Cancer Treatment and Diagnosis	
	A Data Resource for Analyzing and Supporting Blood and Marrow Transplants and Cellular Immunotherapy Research (CIBMTR) (Re-Issue RFA/Coop. Agr./Limited Competition)—Dr. Lori A. Henderson .....	28
	Division of Cancer Treatment and Diagnosis/Office of the Director	
	Patient Derived Xenograft (PDX) Development and Trial Centers (PDTCs) Network (U54) and PDX Data Commons and Coordinating Center (PDCCC) for PDXNet (Re-Issue RFA)—Dr. Jeffrey A. Moscow .....	29
	Systematic Testing of Radionuclides in Preclinical Experiments (STRIPE) (New PAR)—Dr. Michael G. Espey.....	30
	Office of the Director	
	Informatics Technology for Cancer Research (Re-Issue RFA/Coop. Agr)—Dr. Juli Klemm.....	31
XV.	Ongoing and New Business—Drs. John D. Carpten and Keith T. Flaherty .....	32
	NCAB <i>ad hoc</i> Subcommittee on Experimental Therapeutics—Dr. Timothy J. Ley .....	32
	Questions and Answers .....	33
	Other Business—Drs. John D. Carpten and Keith T. Flaherty. ....	33
	Future Agenda Items—Drs. John D. Carpten and Keith T. Flaherty.....	33
XVI.	Adjournment— Drs. John D. Carpten and Keith T. Flaherty .....	34

**TUESDAY, 7 DECEMBER 2021**

**I. NATIONAL CANCER ADVISORY BOARD (NCAB) CLOSED SESSION—DR. SCOTT W. HIEBERT**

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

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

*Dr. Scott Hiebert adjourned the NCAB closed session at 1:11 p.m.*

**WEDNESDAY, 8 DECEMBER 2021**

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

Dr. John D. Carpten called to order the 5<sup>th</sup> 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 1 September 2021 NCAB meeting was approved unanimously.

Dr. Carpten and Dr. Flaherty called Board members’ attention to the future meeting dates listed on the agenda, noting that the 2023 dates will need to be confirmed.

**Motion.** A motion to approve the 2023 NCAB meeting dates was approved unanimously.

**Motion.** A motion to approve the 2023 BSA meeting dates was approved unanimously.

**III. NCI DIRECTOR’S REPORT—DR. NORMAN E. SHARPLESS**

Dr. Norman E. Sharpless, Director, NCI, welcomed members of both the BSA and NCAB to the 5<sup>th</sup> Virtual Joint Meeting of these Boards and reviewed the agenda. He provided an update on activities commemorating the 50<sup>th</sup> anniversary of the National Cancer Act (NCA) of 1971, personnel changes, NCI budget appropriations and paylines, NCI programs and initiatives, and cancer research progress.

Dr. Sharpless introduced the new BSA Chair, Dr. Keith T. Flaherty, Director, Clinical Research, Massachusetts General Hospital Cancer Center, and welcomed new BSA members: **Dr. Chandraknath 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; **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; **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; **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; **Dr. Nelson J. Chao**, Donald D. and Elizabeth G. Cooke Professor, Chief, Division of Hematologic Malignancies and Cellular Therapy/BMT, Director, Global Cancer, Duke University School of Medicine; **Dr. Gloria D. Coronado**, Mitch Greenlick Endowed Scientist in Health Disparities Research, Kaiser Permanente Center for Health Research; **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; **Dr. Shelton “Shelley” Earp**, Director, University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, Director, UNC Cancer Care, University of North Carolina at Chapel Hill; **Dr. Dorothy K. Hatsukami**, Associate Director of Cancer Prevention and Control, Masonic Cancer Center, Professor, Department of Psychiatry, University of Minnesota; **Dr. Trey Ideker**, Professor, Department of Medicine, University of California, San Diego; **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; **Dr. Erle S. Robertson**, Harry P. Schenk Endowed Chair Professor, Vice-Chair, Department of Otorhinolaryngology, University of Pennsylvania School of Medicine; and, **Dr. Richard C. Zellars**, William A. Mitchell Professor and Chair, Department of Radiation Oncology, Simon Comprehensive Cancer Center, Indiana University

Dr. Sharpless also welcomed new NCAB members: **Dr. John D. Carpten**, the NCAB Chair, Professor and Chair, Department of Translational Genomics, Royce and Mary Trotter Chair in Cancer Research, Keck School of Medicine, University of Southern California; **Dr. Nilofer S. Azad**, Professor of Oncology, Co-Director, Developmental Therapeutics Program, Co-Leader, Cancer Genetics and Epigenetics, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University; **Dr. Luis Alberto Diaz, Jr.**, Head, Division of Solid Tumor Oncology, Grayer Family Chair in Medicine, Department of Medicine, Memorial Sloan Kettering Cancer Center; **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; **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; **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; and **Dr. Karen M. Winkfield**, Executive Director, Meharry-Vanderbilt Alliance, Ingram Professor of Cancer Research, Vanderbilt-Ingram Cancer Research, Professor of Radiation Oncology, Vanderbilt University School of Medicine.

Dr. Sharpless acknowledged retiring NCAB members, mentioning that a recognition event would be held later in the meeting, and he expressed appreciation to Dr. Dafna Bar-Sagi, outgoing BSA chair, for her commitment to the NCI over the years and to Dr. Scott W. Hiebert, who served as acting NCAB chair in the past year.

**50<sup>th</sup> Anniversary of the National Cancer Act (NCA) of 1971.** Dr. Sharpless reminded the BSA and NCAB members that the NCI continues to commemorate the 50<sup>th</sup> anniversary of the NCA of 1971, which was signed on 23 December 1971. The NCI has led a national media effort to communicate the importance of the past 50 years of cancer research as a result of the NCA among stakeholders across the cancer community. Further progress for patients is still needed. Dr. Sharpless attended an NCA-50 event held at the Nixon Presidential Library, during which discussions focused on the visionary aspects of the NCA and how it established new principal authorities and additional funding for cancer research. The NCA has enabled the Surveillance, Epidemiology, and End Results (SEER) database, NCI-Designated Cancer Centers (Cancer Centers), NCI Clinical Trials Network, and more recent, more modern capabilities. Although the impact has been significant, the notion of curing cancer within 5 years of the Act’s passing was ambitious. Cancer has proved to be a much more challenging biological problem than

envisioned. Finding a cure for cancer is a leading priority for the Biden Administration, and the field has some distance to advance in addressing the burden of cancer in modern American life.

Other groups have joined in this media campaign to highlight the opportunities for future progress in cancer research. For example, the U.S. Food and Drug Administration (FDA) hosted the “50 Years of Progress in Treating Patients with Cancer” event led by Dr. Richard Pazdur, Director, FDA Oncology Center of Excellence. On 13 December 2021, Dr. Sharpless will speak at the “50 Years and Counting: Engaging the Generations on Future Cancer Equity Opportunities” event. Dr. Sharpless noted how important it is for patients and patient advocates to hear these messages and for Congress to hear from cancer research stakeholders. He commented that the NCA-50 is not just about the NCI; it is about everyone who has an investment in cancer research, from academia to industry to nonprofit organizations and advocacy to philanthropy. In a recent NCA-50 outreach activity, the NCI encourages members of the cancer research community to share their vision for the future of cancer research. Participants can post a 15- to 30-second video clip on social media, answering the prompt “Ending cancer as we know it means...” using the hashtag #NothingWillStopUs, #NadaNosDetendrá.

**COVID-19 Related Activities.** On 2 December 2021, President Joseph Biden visited the NIH, and his remarks focused on the NIH response to the COVID-19 pandemic and ways of addressing recent developments on this topic (e.g., the Omicron variant). BSA and NCAB members were reminded of the NCI COVID-19-related research portfolio, including the Serological Sciences Network (SeroNet), efforts led by the Frederick National Laboratory for Cancer Research (FNLCR), and the NCI COVID-19 in Cancer Patients Study (NCCAPS). He noted that special supplemental funds of \$306 million (M), separate from the regular NCI appropriations, have supported COVID-19-related research.

The American Rescue Plan, signed into law in March 2021, included a \$48.7 billion (B) appropriation to the U.S. Department of Health and Human Services (HHS) to detect, diagnose, trace, and monitor SARS-CoV-2 infection to mitigate the spread of COVID-19. The HHS allotted \$63 M to the NCI to address two additional key priorities: a peripheral blood samples project (\$50 M) and a vaccine trial (\$13M) evaluating immunocompromised individuals, especially patients with cancer. This additional funding will support the following COVID-19 activities: developing serology assays for detecting SARS-CoV-2 antibodies, generating reference materials and standards for clinical trials and vaccine licensing, and conducting surveillance studies. The FNLCR coordinates most of the NCI’s COVID-related research and works collaboratively with external partners. Dr. Sharpless noted that the unique expertise and capabilities of the NCI positions the Institute to respond to the public health crisis associated with the COVID-19 pandemic. He conveyed the NCI’s gratitude for the trust placed in it by HHS and Congress to advance serology science.

**The Role of the NCI in Ending Cancer.** Dr. Sharpless remarked that the NCI remains cancer focused and works closely with the White House Office of Science and Technology Policy (OSTP) on new cancer plans. He announced that Dr. Henry Rodriguez, Founding Director, NCI Office of Cancer Clinical Proteomics Research, is on detail to the OSTP. As Assistant Director for Strategic Health and Cancer Science, Dr. Rodriguez will lead strategies in cancer and other diseases that include advancing innovations to improve health for all Americans.

Discussing cancer mortality, Dr. Sharpless explained that cancer kills 600,000 people per year in the United States, of whom nearly 1,800 are age 19 and younger. Although the cancer mortality rate has declined over the years, implementing reasonable measures can further accelerate this trend. He called attention to several true statements about cancer in the United States that the NCI is seeking to reverse. Too few methods are available to prevent cancer. Many types of cancer lack effective approaches to early detection and diagnosis. Stark inequities exist in diagnosis, treatment and trial access, and patient outcomes based on race, region, and resources. Too many patients and families are left to navigate the disease on their own. Curative therapies come at the cost of serious side effects. Success in some of the toughest to treat and rare cancers is limited. Dr. Sharpless emphasized six broad themes to accelerate the



decline/end of cancer mortality: (1) build on 50 years of progress, (2) advance health equity, (3) personalize cancer care, (4) embrace technology and innovation to learn from every patient, (5) inspire the next generation of diverse researchers, and (6) prepare for challenges of the future.

**NCI Budget Appropriations and Paylines.** Dr. Sharpless reported on the NCI budget and interim paylines. The NCI regular appropriations have increased steadily since fiscal year (FY) 2015. The FY 2021 budget continues the appropriations for the Cancer Moonshot<sup>SM</sup> and Childhood Cancer Data Initiative (CCDI). The FY 2022 President's budget was released in May 2021, and the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS) passed its bill out of committee in June 2021. The Senate Appropriations Subcommittee on Labor-HHS has not released its bill, and approval of the FY 2022 spending budget is pending. The federal government is operating under a continuing resolution (CR) that funds the government through 18 February 2022. Dr. Sharpless noted that Ms. M.K. Holohan, Director, Office of Government and Congressional Relations (OGCR), NCI, will provide further details on the NCI FY 2022 budget and other legislative affairs later in the meeting.

Dr. Sharpless announced that the NCI has tentatively established interim paylines for FY 2022: 9<sup>th</sup> percentile for R01 grants to established and new investigators, 14<sup>th</sup> percentile for R01 grants to early-stage investigators (ESIs), and 9<sup>th</sup> percentile for exploratory grants (R21). Non-competing grants will be funded at the 90 percent level. Further details have been provided on the NCI blog, *NCI Bottom Line: A Blog About Grants and More*.

**NCI Programs and Initiatives.** Dr. Sharpless reported that the CCDI, in the second year of its 10-year funding plan, is progressing at a steady pace. This Initiative seeks to create an infrastructure and a community to aggregate and use data from every child with cancer in the United States. The CCDI Annual Symposium, held on 9 November 2021, was well attended. Dr. Sharpless highlighted progress of two components of the CCDI. First, the Childhood Molecular Characterization Protocol, which builds on Project:EveryChild, is open to all children with cancer regardless of treatment facility or location. The aim is to gather clinical and molecular information from every child with cancer, with the goal of characterizing approximately 3,000 children with hard-to-treat cancers. The NCI will support the sequencing analysis to be performed by a Clinical Laboratory Improvement Amendments (CLIA)-accredited laboratory. The Protocol launch is anticipated for spring 2022, and the Children's Oncology Group (COG) and Biopathology Center at Abigail Wexner Research Institute at Nationwide Children's Hospital will be responsible for specimen handling. Second, the National Childhood Cancer Registry (NCCR)—an effort that integrates data from registries, hospitals, research centers, and insurers—will generate an accurate total of cancer cases. The NCCR will generate an expanded database consisting of genomic and tumor characteristics, treatment information, and disease recurrence indicators. A new interactive online cancer statistics tool, the NCCR\*Explorer, was recently launched and provides comprehensive incident survival statistics based on the International Classification of Childhood Cancer.

On 10 June 2021, President Biden and U.K. Prime Minister Boris Johnson revitalized the 80-year Atlantic Charter and issued a joint statement committing to international bilateral cooperation in cancer research. On 13–14 November 2021, the first U.S.–U.K. Bilateral Cancer Summit was convened, and representatives (e.g., researchers, patients, other stakeholders) from the cancer research communities of both nations attended. Summit participants discussed six thematic topics, some of which crosscut what the NCI hopes to reverse in terms of what is true about cancer in the United States. A U.S.–U.K. Bilateral Leadership Summit is planned for spring 2022. These efforts have largely been led through the NCI Center for Global Health (CGH), which just celebrated its 10<sup>th</sup> anniversary.

**Breast Cancer and Environmental Carcinogens.** Dr. Sharpless explained that environmental carcinogens are an ongoing public concern, and scientific interest in this topic is overwhelming, particularly for breast cancer. Copious new data, new approaches, and new toxic chemicals in the

environment that may be significant and are present in consumer products and drinking water speak to the need for research in this area.

The NCI and the National Institute of Environmental Health Sciences (NIEHS) hosted a meeting focused on breast cancer and the environment in May 2021 to discuss the evolving science and opportunities to advance work in this area. Workshop participants highlighted successful approaches and identified new technologies and approaches to be further studied, such as mutational signatures and highly sensitive mass spectrometry analyses. A workshop summary is posted online and can be accessed from the NCI website. Dr. Sharpless and the NIEHS Director, Dr. Richard Woychik, have discussed common goals in addressing challenges of breast cancer and environmental carcinogens that would be applicable to any cancer and are planning future activities.

**Ongoing Activities.** The U.S. Preventive Services Task Force (USPSTF) revised its lung cancer screening recommendations to expand eligibility to include a greater number of smokers. In a report published in the October 2021 issue of the *Journal of Thoracic Oncology*, the authors evaluated the effect of joint lung cancer screening and tobacco cessation interventions with the new USPSTF eligibility revisions. This report highlighted that cancer screening is underutilized and that increasing it would improve lung cancer mortality nationally. Combining tobacco cessation programs with lung cancer screening could be highly impactful. In fact, modeling data suggest that lung cancer screening within the 40<sup>th</sup> to 50<sup>th</sup> percentile levels and joint tobacco cessation efforts could have a significant effect on the health of Americans.

The FDA recently approved belzutifan for the treatment of renal cell carcinoma, specifically von Hippel–Lindau (VHL) tumors. Belzutifan, an active drug in treating advanced renal cancer, targets hypoxia-inducible factor alpha that is activated in VHL-deficient tumors. Dr. Sharpless commented on this example of basic science that translates into an agent for the public good, noting that this advance resulted from years of NCI support. In the Intramural Research Program, Dr. W. Marston Linehan co-discovered the VHL tumor suppressor gene, and Dr. Richard Klausner and colleagues conducted renal cancer research and contributed discoveries in this field. Extramural-funded investigators Drs. William G. Kaelin, Jr. and Gregg L. Semenza won the Nobel Prize (shared with Dr. Peter Ratcliffe) for their discoveries in understanding how VHL contributes to oxygen sensing and target activation.

Dr. Sharpless called attention to new and ongoing clinical trials. Specifically, a Phase IB/II clinical trial evaluating the Nouscom-209 (Nous-209) vaccine for recurrent neoantigen immunogenicity and cancer immune interception in patients with Lynch syndrome is anticipated to open mid-March 2022. Extramural investigators at MD Anderson Cancer Center collaborated with the NCI to develop the Nous-209 preventative vaccine for individuals at high risk for colon cancer. Also, a Phase I trial, led by Sidney Kimmel Comprehensive Cancer Center, for patients who are at high risk of pancreatic cancer will examine mutant Kirsten rat sarcoma (KRAS), targeted long peptide vaccine. Dr. Sharpless noted that Dr. Elizabeth Jaffee is the PI for this trial. Additionally, the NCI-COG Pediatric Molecular Analysis for Therapy Choice (MATCH) trial enrollment will pause after 31 December 2021, when the tumor screening process for the standard of care changes to use commercial laboratories, whereas the Pediatric MATCH trial is tentatively scheduled to resume in March 2022. Once resumed, treating physicians may send their patients' tumor samples to any CLIA-accredited laboratory for genomic sequencing. Six treatment arms will continue to enroll participants.

Lastly, Dr. Sharpless highlighted that the NCI Equity and Inclusion Program (EIP), overseen by the NCI Equity Council, is launching the Early Investigator Advancement Program (EIAP) for the advancement of scientists from diverse backgrounds. Applications are due by 31 December 2021, and the target start date will be 1 March 2022. A pre-application webinar will be held on 9 December 2021.

## Questions and Answers

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Department of Medicine, Washington University School of Medicine in St. Louis, asked whether the paylines were permanent and whether Research Project Grants (RPGs) that are funded between the 9<sup>th</sup> and 11<sup>th</sup> percentiles would be reconsidered when the FY 2022 budget is passed. Dr. Sharpless confirmed that the paylines are conservative and temporary and will be in effect until the FY 2022 budget and appropriations are more certain. He noted that the NCI also supports grants using select pay.

Dr. Anna D. Barker, Chief Strategy Officer, Ellison Institute for Transformative Medicine, University of Southern California, asked about the effect of the reduction in paylines on the NCI goals to reach the 15<sup>th</sup> percentile payline by 2025 and the status of the Advanced Research Projects Agency for Health (ARPA-H) initiative. Dr. Sharpless informed members that without increasing support from Congress, which is necessary in terms of raising the regular budget appropriations, the NCI likely will pause its payline goals. He also noted that discussions are ongoing about the budget and where in the NIH ARPA-H (a high priority for the Biden Administration) would reside; ARPA-H will require an independent director.

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

Ms. Holohan provided a brief report on the overall appropriations bills, FY 2022 budget, and other legislation of interest, including spending requests. She called attention to the detailed legislative report contained in the Board meeting book and noted events that transpired in the past 24 hours. The debt limit had to be either raised or suspended by 15 December 2021; this has historically been a bipartisan responsibility. Raising the debt limit was not linked to the budget resolution and had to be voted on separately. Ms. Holohan explained that use of budget reconciliation for budget resolutions allows a quick legislation process that cannot be filibustered. A deal was reached in the majority party, a one-time exemption, until the midterm elections in November 2022. The new debt limit is estimated to be in the \$2 trillion range.

Congress must address multiple fiscal deadlines this year, including the debt ceiling, FY 2022 budget and appropriations, and other key programs set to expire at the end of FY 2021. Ms. Holohan echoed Dr. Sharpless regarding the federal government operating under a CR for the second time this fiscal year. All bills can either be introduced in a large omnibus package or in one to two minibuses of specific combined bills. Negotiations on the \$1 trillion bipartisan infrastructure bill (passed in August 2021), FY 2022 \$3.5 trillion budget resolution, and Build Back Better (BBB) package have diverted legislators' attention from the regular appropriations work.

On 16 November 2021, the \$1 trillion bipartisan infrastructure bill (Investing in a New Vision for the Environment and Surface Transportation [INVEST] in America Act, H.R. 3684) was signed into law by President Biden. INVEST includes traditional provisions (e.g., universal pre-kindergarten, childcare tax credits, strengthening of the U.S. medical supply chain) and innovative provisions, such as high-speed internet and telehealth. Next on the priority list for the Biden Administration is the human infrastructure bill, the BBB Act (H.R. 5376), on which a vote is anticipated prior to the House and Senate recess for the 25 December 2021 holiday. A draft version of the 21st Century Cures 2.0 Act (Cures 2.0) was released in June 2021 and introduced to the House in November 2021. Cures 2.0 would establish ARPA-H within the NIH, authorize research funding, address clinical trial diversity and access, expand and study telehealth, improve access to diagnostics and treatment, and appropriate funds for additional patient and caregiver training and education.

The President's FY 2022 budget request (which starts the NIH/NCI budget process) includes \$52 B for the NIH (a \$9 B increase), which includes \$6.5 B for ARPA-H and \$6.7 B for the NCI (a \$174 M increase). The House Appropriations Subcommittee on Labor-HHS passed its bill out of

committee in June 2021 and included \$49 B for the NIH (a \$3.5 B increase for the NIH with \$3 B designated for ARPA-H) and \$6.99 B for the NCI (a \$434 M increase). The Senate Appropriations Subcommittee on Labor-HHS has not released its bill. The House passed a minibuss appropriations package containing seven bills, including the Labor-HHS bill. BSA and NCAB members were reminded that Congress has enacted one or more CRs in all but three of the last 44 fiscal years.

Ms. Holohan announced that the FY 2022 appropriations, after 11 years, returned Congressional earmarks on House appropriation bills. To date, 326 Representatives (221 Democrats and 105 Republicans) submitted 2,978 Community Project Funding requests for FY 2022, totaling just over \$7 M. A total of 64 senators (45 Democrats, 2 Independents, and 17 Republicans) submitted 8,007 Congressionally Directed Spending requests for FY 2022, totaling \$27.6 M. In addition, the House passed the defense authorization bill, a bipartisan priority that has been in effect for more than 60 years. The defense bill, which is \$25 M greater than the President's budget request, called attention to a disagreement about appropriations and defense spending. Issues yet to be resolved concern the Hyde Amendment and Budget Control Act.

Ms. Holohan closed her presentation by reflecting on the life and political career of the late Senator Robert J. Dole (R, Kansas), who was the longest serving Senator in office, from 1960 to 1996. Senator Dole, known as a bipartisan debater, worked with other senators to extend the solvency of the Social Security system in 1983 and pass the Americans with Disabilities Act in 1990.

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

On behalf of the NCI, Dr. Sharpless recognized the contributions made by members of the NCAB whose terms of office have ended. He expressed appreciation for their service and dedication over the course of their terms. Those retiring NCAB members are: **Dr. Peter C. Adamson**, Global Head, Oncology Development and Pediatric Innovation, Sanofi; **Dr. Deborah Watkins Bruner**, Senior Vice President for Research, Robert W. Woodruff Professor in Nursing, Emory University; **Dr. Yuan Chang**, American Cancer Society Research Professor, Distinguished Professor of Pathology, University of Pittsburgh School of Medicine (UPMC), Chair of Cancer Virology Hillman Cancer Center, UPMC; **Dr. Timothy J. Ley**, Professor of Medicine and Genetics, Division of Oncology, Department of Medicine, Washington University School of Medicine in St. Louis; and **Dr. Max S. Wicha**, Madeline and Sidney Forbes Professor of Oncology, Director, Forbes Institute for Cancer Discovery, Founding Director Emeritus, University of Michigan Rogel Cancer Center, Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan.

#### VI. CANCER MOONSHOT<sup>SM</sup>: LOOKING AHEAD—DR. DINAH S. SINGER

Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development, NCI, described Cancer Moonshot<sup>SM</sup> achievements during the past 5 years and looked ahead to how the NCI plans to sustain and build on those accomplishments, incorporating them into the larger cancer research effort.

**Cancer Moonshot<sup>SM</sup> Goals, Implementation, and Achievements.** Dr. Singer noted that the legislation that enacted this initiative had three specific goals: Goal 1, accelerate progress in our understanding of cancer; Goal 2, enhance data sharing; and Goal 3, encourage greater cooperation and collaboration.

To achieve Goal 1, the NCI convened and charged an NCAB Blue Ribbon Panel (BRP) to identify those areas of research poised for acceleration, and the BRP identified 10 recommendations. Dr. Singer highlighted the Cancer Moonshot<sup>SM</sup> initiatives that implement those recommendations. The patient engagement recommendation necessitated networks to help patients with cancer find clinical trials and help researchers enroll patients from diverse populations. Two such networks, NCI Comprehensive Oncology Network Evaluating Rare CNS Tumors (NCI-CONNECT) and My Pediatric and Adult Rare

Tumor (MyPART), started in 2018 and have formed partnerships among patients, advocates, and health care providers aimed at understanding and treating rare tumors. The NCI-CONNECT and MyPART networks also have activated clinical trials. In 2020, the Patient Engagement and Cancer Genome Sequencing (PE-CGS) Network launched. Its goals are twofold: encourage patients with cancer and cancer survivors to actively participate in cancer research and address gaps in knowledge of cancer genomics of rare or highly lethal cancers and cancers in understudied populations.

Pediatric cancer transverses two recommendations: immunotherapy network and drivers of childhood cancers. The Fusion Oncoproteins in Childhood Cancers (FusOnC2) consortium/network focuses on understanding the structure and function of fusion onco-protein complexes to inform the development of small-molecule disruptors. The Pediatric Immunotherapy Discovery and Development Network (PI-DDN), established as a preclinical research network to develop novel immunotherapy approaches for pediatric cancer, has been very successful. For example, one program has generated a class of chimeric antigen receptor (CAR) T-cells that target intracellular onco-proteins by recognizing surface onco-peptide human leukocyte antigen complexes. The Pediatric Cancer Immunotherapy Trials Network (CITN) supports multi-institutional Phase I and early Phase II pediatric immunotherapy trials.

Immunotherapy also has been a major focus for adult cancers. The Immuno-Oncology Translational Network (IOTN) focuses on ways to optimize and harness the adult immune system for more effective immunotherapies by understanding the immune mechanisms that contribute to tumor regression, progression, and resistance. IOTN investigators have developed a CAR T-cell that kills cancer cells expressing large amounts of a non-mutated target antigen, while sparing normal cells that express lower levels of the same protein, increasing on-target killing but reducing off-tumor killing.

Implementation science has been a major focus of the recommendations on prevention and detection strategies and symptom management. One such program implemented in these areas has been Improving the Management of symPtoms during and following Cancer Treatment (IMPACT), which focuses on reducing symptom burden and optimizing therapeutic outcomes in children and adults. The Cancer Center Cessation Initiative (C3I) has led to a better understanding of what constitutes a successful smoking cessation program for patients with cancer and cancer survivors. Other programs on these topics, such as Accelerating Colorectal Cancer Screening and follow-up through Implementation Science (ACCSIS), are increasing colorectal cancer screening, follow-up, and referral in underserved groups. Dr. Singer emphasized that during the pandemic these teams continued work on implementing novel telehealth services that led to increased screening uptake. ACCSIS and other colorectal cancer screening programs supported by this Initiative explicitly address health disparities—a crosscutting theme of the BRP recommendations and Cancer Moonshot<sup>SM</sup> agendas.

The recommendation on generating human tumor atlases led to establishing the Human Tumor Atlas Network (HTAN). This Network is developing three-dimensional atlases that visualize the architecture, composition, and multiscale interactions of tumor progression and metastasis. Data from eight initial atlases, including pediatric graphics, are available through the HTAN data portal, with additional information to be added soon.

Dr. Singer summarized that from 2017 to the present, the Cancer Moonshot<sup>SM</sup> has supported 70 programs and initiatives across 240 projects. In parallel, she noted that the NCI has been addressing the Cancer Moonshot<sup>SM</sup> Goals 2 and 3. Regarding Goal 2, the NCI has developed the Cancer Research Data Commons (CRDC), which houses and will readily make available all Cancer Moonshot<sup>SM</sup> data. In addition, all Cancer Moonshot<sup>SM</sup>-funded publications and underlying data are required to be made publicly available (i.e., open access) immediately upon a publication's acceptance. To implement Goal 3, the NCI has ensured that collaboration remains integral to and is embedded within the Cancer Moonshot<sup>SM</sup> programs and networks. The NCI has established partnerships with other NIH Institutes and other federal agencies, including the U.S. Departments of Energy (DOE), Defense (DoD), and Veterans Affairs (VA). In addition, Cancer Moonshot<sup>SM</sup>-wide collaborative meetings have brought together

investigators from across the funded programs (e.g., HTAN, IOTN, PI-DDN) to discuss their research and to spark cross-initiative alliances. Last, the monthly Cancer Moonshot<sup>SM</sup> Seminar Series is designed to inform the research community and the public of the research accomplishments.

**Cancer Moonshot<sup>SM</sup> Assessment.** Dr. Singer explained that as the Cancer Moonshot<sup>SM</sup> comes to the end of its 7-year funding period in FY 2023, the NCI has begun to assess its contributions using a two-phase approach. Phase 1, which is Data Collection, Monitoring, and Interim Reporting will focus on collecting and analyzing data to monitor progress and will continue through FY 2026, when the initial funded grants will end. Phase 2, Final Assessment, will be ongoing during the following 2 years into FY 2028. An early analysis of accomplishments shows that the Cancer Moonshot<sup>SM</sup> has been productive and has resulted in 1,212 publications, 14 patents, and 22 clinical trials. Cancer Moonshot<sup>SM</sup> publications, on average, are more highly cited than other NCI-supported research, indicating a high overall impact. The Cancer Moonshot<sup>SM</sup> also has expanded the cancer research workforce. Of the Cancer Moonshot<sup>SM</sup>-funded investigators, 25 percent were new investigators, and more than 10 percent had no prior NCI funding. Women represented approximately one-third of all of investigators, which reflects the representation in the applicant pool. This assessment illustrates that the Cancer Moonshot<sup>SM</sup> has laid critical foundations for future advances.

**Looking Ahead.** Beyond FY 2023, Dr. Singer indicated that the NCI is beginning to explore ways to incorporate the Cancer Moonshot<sup>SM</sup> scientific advances into the overall NCI portfolio and transition the special 7-year funding to standard, appropriated funding. The NCI will need to build on foundational scientific advances, explore new areas and opportunities that have emerged, continue to encourage collaborative science to complement investigator-initiated research, and make data sharing and open access publication routine across cancer research. During this transition, the NCI first will determine which programs, including the developed infrastructure, require continued support to accomplish their goals. The next steps will be to develop and support new programs that have emerged as a result of the funded programs and balance the needs of Cancer Moonshot<sup>SM</sup>-related programs with non-Cancer Moonshot<sup>SM</sup> programs. After understanding the demand, the NCI will establish a transition plan to ease those Cancer Moonshot<sup>SM</sup>-funded programs into appropriated funding.

Dr. Singer reviewed a summary of the programs requesting continuation. Of the 70 programs and initiatives across the 240 projects, two-thirds have expressed interest in continuing beyond their estimated end dates. These will need to be supported through standard appropriated funds. Because the Cancer Moonshot<sup>SM</sup> initiatives began in different fiscal years, the impact of the budget extends from FY 2022 to FY 2027, with the greatest effect occurring between FY 2023 and FY 2024. Dr. Singer called attention to the budget challenges that the NCI must address. The total Cancer Moonshot<sup>SM</sup> appropriation was \$1.8 B, of which \$1.25 B has been obligated to the existing programs and \$334 M has been committed to additional programs. The requests for continuation total \$884 M, leaving an estimated deficit of \$564 M.

In anticipation of having to support Cancer Moonshot<sup>SM</sup> programs funded at later years in the 7-year cycle, the NCI has reserved \$280 M no-year funds to ease the transition into appropriated funding. Using budget modeling, the NCI estimates that \$100 M will need to be added to the NCI budget annually to support the programs requesting continuation. Dr. Singer emphasized that those requests would go through the normal approval process, and likely not all will be approved. The budget modeling will be adjusted as scientific concepts emanating from the continued Cancer Moonshot<sup>SM</sup> programs are developed and introduced.

Regarding scientific areas supported by the Cancer Moonshot<sup>SM</sup> and the associated investments, the major spending has been in prevention and early detection, immunotherapy, childhood cancers, and infrastructure. The requests for continuation primarily represent both research and infrastructure, with a greater emphasis on infrastructure. This information will help inform the NCI's decisions on prioritizing continued support for Cancer Moonshot<sup>SM</sup>-related programs. Even with the budgetary challenges, Dr. Singer explained that the NCI will continue to move forward with this transition plan, informed by the

ongoing assessment of the respective programs. In closing, Dr. Singer expressed appreciation to the NCI staff serving on the Cancer Moonshot<sup>SM</sup> Implementation Teams for their efforts and ongoing commitment to the success of this Initiative.

### **Questions and Answers**

Dr. Heimberger asked about plans to evaluate the differences in using the Cancer Moonshot<sup>SM</sup> funding strategy compared with the NCI's standard funding distribution practices. Dr. Singer replied that the NCI research funded-base (investigator-initiated) is used as a comparator in the data analysis of metrics but is not ideal because the Cancer Moonshot<sup>SM</sup> funding is supporting networks and cooperative agreements. The NCI is working to determine the best approach for the assessments.

Dr. Singer clarified that the Cancer Moonshot<sup>SM</sup> set-aside funds were designed by the NCI to transition programs and minimize the impact on the RPG pool and paylines, and she noted that NCI investigators are aware that this funding will end.

Dr. Michael John 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, pointed that the Cancer Moonshot<sup>SM</sup> goals of data sharing were intended to be accomplished through the CRDC and asked about the reporting of individual data-sharing pipelines across the funded programs. Dr. Singer explained that some of the programs have their own data coordinating centers designed to directly deposit data to the CRDC. Dr. Becich suggested a presentation on the various Cancer Moonshot<sup>SM</sup> data pipelines at a future BSA and NCAB meeting. Dr. Sharpless added that the NCI also could consider an update on the progress of the CRDC at a future meeting.

### **VII. THE NIH COMMON FUND: FACULTY INSTITUTIONAL RECRUITMENT FOR SUSTAINABLE TRANSFORMATION (FIRST) PROGRAM—DR. SANYA A. SPRINGFIELD**

Dr. Sanya A. Springfield, Director, Center to Reduce Cancer Health Disparities (CRCHD), provided an update on the NIH Common Fund (CF) initiative, FIRST, which the NCI has been helping to administer. She acknowledged Dr. Carpten as the first African American to serve as Chair of the NCAB and expressed appreciation to the NCI and Dr. Sharpless for his nomination to this illustrious position.

Dr. Springfield reminded the BSA and NCAB members that NIH Roadmap launched in 2004 and was unanimously reauthorized by Congress in 2006 at the NIH level, to establish the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) and the NIH CF to provide a dedicated source of funding to enable goal-driven NIH-wide research. To be considered for funding, NIH CF programs must meet five criteria: They must be transformative, catalytic, synergistic, crosscutting, and unique. The FY 2021 NIH CF programs span the categories of new types of clinical partnerships; data, tools, and methods; new paradigms; and transformative workforce support. NCI leadership and staff are involved in many of the NIH CF initiatives.

Discussing the challenges and opportunities that highlight the need for transformative workforce support, Dr. Springfield remarked that underrepresented minorities are being awarded doctoral degrees, but many are not being hired at academic institutions. Many of those who are hired report feeling a sense of isolation and lack of trust in work relationships compared with their non-minority counterparts. In addition, academic institutions lack the necessary elements of inclusion and equity in science. To address these challenges, then-NIH Chief Officer for Scientific Workforce Diversity, Dr. Hannah A. Valantine,

proposed the FIRST concept to the Advisory Committee to the Director, which was subsequently approved by the DPCPSI Council of Councils.

FIRST consists of two components: a Faculty Cohort (U54) and Coordination and Evaluation Center (CEC) (U24) managed by the NCI and National Institute on Minority Health Disparities (NIMHD), respectively. The initial program budget allocation of \$241 M spans 9 years from FY 2021 through FY 2029. The purpose of the FIRST U54 Cohort is to transform the culture at NIH-funded extramural institutions and provide support for these institutions to implement, enhance, and sustain cultures of inclusive excellence. Dr. Springfield emphasized that the aim is to create environments in which all individuals are welcome, not only to survive, but also thrive. The NCI provides support to institutions to recruit and hire a diverse cohort of early-career faculty in clusters of no less than three. The recruited faculty must have demonstrated a strong commitment to promoting diversity and inclusive excellence and be competitive for an advertised research tenure-track (or equivalent) faculty position.

The FIRST program will sponsor 12 staggered 5-year awards (i.e., four awards annually). Contingent on the availability of funds, an RFA will be issued each year for 3 years. The launch during the first year will focus on planning for key personnel and core leaders, strategies for inclusive excellence, cluster hiring, faculty professional and research development, and search committees, whereas the second through the fourth years are designed for faculty cohort/cluster hiring start-up packages and for professional development and inclusive excellence activities. The final and fifth year will focus on continued activities in the three cores: administration, faculty development, and evaluation. In terms of eligibility, applicant institutions must conduct research in the NIH mission areas and provide evidence of commitment to diversity and inclusion. Applicants also must apply either as a limited-resourced institution (LRI), highly resourced institution (HRI), or within a partnership. An LRI is defined as having received less than \$50 M per year and less than \$25 M per year in NIH R01 total cost support in the 3 years prior to submitting the agreement. An HRI has received more than \$50 M in annual NIH funds within the 3 years prior to the date of submission. A partnership that includes an HRI must hire no fewer than 10 new faculty and no fewer than 6 new faculty with two LRIs.

Dr. Springfield informed BSA and NCAB members that the overall goals and specific measurable objectives of FIRST would be refined over time. She noted that the FIRST Faculty Cohort budget is \$10.2 M for each award, and the institutional financial commitment will be essential to the success of these programs. The NCI received a robust response to the RFA, and FY 2021 FIRST Cohort awardee institutions were announced in September 2021. These include Cornell University (HRI), Drexel University (HRI), Florida State University (LRI), Icahn School of Medicine at Mount Sinai (HRI), San Diego State University (LRI), and The University of Alabama at Birmingham/Tuskegee University (partnership). The grantee kickoff meeting was held in October 2021. Applications have been received and are being reviewed for FY 2022, and an RFA is planned for FY 2023.

### **Questions and Answers**

Dr. Doubeni expressed his enthusiasm for the FIRST program and asked about the extent to which new faculty were being recruited, with attention given to the potential strain on LRIs that could lose their talent pool to the FIRST-funded institutions. Dr. Springfield replied that one aim is to prepare the LRIs, and she does not have a concern that FIRST would lead to an increased number of underrepresented minorities' being taken into mainstream institutions, especially when the implemented FIRST programs begin to increase diversity.

### **VIII. CHALLENGES AND OPPORTUNITIES IN CANCER CONTROL AND POPULATION SCIENCES—DR. ROBERT T. CROYLE**

Dr. Robert T. Croyle, Senior Advisor, and former Director, Division of Cancer Control and Population Sciences (DCCPS), NCI, provided an update on the Division, major programs and initiatives,



essential research infrastructure, and health disparities. The DCCPS began in 1997, and Dr. Barbara Rimer was appointed as its first Director. Programs were formed and continued to evolve over the years, and branches were subsequently established.

**Centers of Excellence Initiatives.** Dr. Croyle noted that one strategy for the Division is to use Centers of Excellence as a research funding mechanism to provide ambitious research goals in a complex and challenging area of great importance to cancer control. In 1999, the first center, Transdisciplinary Tobacco Use Research Centers, was a collaborative effort with the National Institute on Drug Abuse (NIDA) and Robert Wood Johnson Foundation. Since then, seven Centers of Excellence initiatives have been implemented, all collaborative, representing the largest RFAs launched by DCCPS and highlighting some of the highest research priorities in cancer control. The Centers on Telehealth Research and Cancer-Related Care initiative, recently reviewed by the BSA, demonstrates the NCI's signature leadership role at the NIH in telehealth. The lessons learned and key themes from the program evaluation of the Centers of Excellence include team formation, leadership, communication and coordination, training, and institutional policies and structure. The DCCPS subsequently established a new field known as the Science of Team Science, and the National Academies of Sciences, Engineering, and Medicine has published a book on the topic that summarizes the empirical evidence and research on what makes effective teams.

**Cancer Control's Most Important Challenge: Tobacco Control.** Progress in tobacco control remains one of the most significant public health success stories during the last century. Tobacco and cigarette consumption in U.S. adults significantly decreased from 1990 to 2007; this decline has been associated with a number of signature scientific and policy events, all of which were hard fought and hard won. Major progress against cancer has resulted from the advancements in reducing tobacco use, notably the decrease in lung cancer mortality due to reduced tobacco use. Improvements in survival as a result of advancements in therapy also have been remarkable.

Tobacco use and control is not just a cancer issue but is associated with many different chronic diseases, thus underscoring the need for a collaborative interagency effort. The FDA, other NIH Institutes and Centers (ICs), such as the National Heart, Lung, and Blood Institute (NHLBI), NIDA, and HHS have played a key role, along with the Centers for Disease Control and Prevention (CDC) Office on Smoking and Health, and have been close collaborators with the DCCPS/NCI over the years. Dr. Croyle described the DCCPS's key efforts and challenges related to tobacco control for the DCCPS, which include informing the FDA's ability to regulate tobacco products, including nicotine levels; improving the efficacy and effectiveness of cessation programs for teens and young adults; focusing on low socioeconomic status populations; and resolving the electronic (e)-cigarette debate. He reminded BSA and NCAB members that the FDA Center for Tobacco Products funds many of the DCCPS grants on this topic.

Regarding future challenges, Dr. Croyle called attention to a recent report (Avery *et al.*, 2021) that overall cancer trends indicate that mortality reduction in cancer during the last several years has been in the non-obesity-associated cancers. These findings serve as a warning moving forward, highlighting the threat of obesity in challenging progress against cancer in the United States.

**Essential Infrastructure for Population Science.** Dr. Croyle and the DCCPS have focused attention on building and enhancing the research infrastructure for population science in the United States. One primary effort has been establishing cancer epidemiology cohorts and consortia. The Division supports several cancer epidemiology cohorts, which are essential infrastructure for cancer research and have been a model of collaboration and data sharing. Cohort studies have enabled and produced the statistical power necessary for molecular epidemiology and understanding gene-environment interaction and risk factors. Dr. Croyle noted that two PARs related to epidemiology cohorts will be presented to the joint Boards later in the meeting.

**Cancer Surveillance.** Dr. Croyle remarked on the success of SEER, noting that Dr. Lynne Penberthy, Associate Director, Surveillance Research Program (SRP), DCCPS, provided a detailed update on the SEER program during the 14–15 June 2021 BSA and NCAB meeting. One of his goals as DCCPS Director, Dr. Croyle explained, was to expand the SEER program by the 50<sup>th</sup> anniversary of the NCA to provide coverage that represents 50 percent of the U.S. population. On 1 June 2021, the DCCPS reached this goal. Two tiers of SEER contracts are in place to support registries: traditional, full research support contracts and smaller agreements to support research entities. The smaller contracts establish a mechanism that enables those sites to participate in special research projects across the SEER system. Dr. Croyle acknowledged the CDC National Program of Cancer Registries, which has been a close collaborator with the DCCPS, especially in the new Childhood Cancer Registry initiative. Some states (e.g., Texas) recently added to SEER diversify who is enrolled and registered in SEER.

To represent real-world data at the population level, SEER needed to expand. The significant changes in demographics in the United States today continue to be underappreciated by policymakers, scientists, and the academic community. The growth of the U.S. Latino population, for example, deserves more attention from the scientific community. The United States is lagging in generating the subpopulation-relevant evidence needed to better understand genetic epidemiology, as well as the effects of environmental exposures. With the SEER expansion, Hispanic population enrollment in the cancer registries has increased. The diversity of Asian American subpopulations represented in SEER also has undergone a significant change. This new expansion of research infrastructure is in the early stages and will continue during the next year. Dr. Croyle anticipates that this change will enable future population science research, as well as clinical and basic science research.

The surveillance program reaches beyond cancer incidence. The NCI leads or co-sponsors many national surveys that are critical components of surveillance. One such example is the Health Information National Trends Survey (HINTS), which monitors, at a national level, what the public thinks and knows about cancer, as well as myths about it.

**Leveraging NCI-Designated Cancer Centers for Cancer Control.** Dr. Croyle explained the use of the DCCPS discretionary budget to focus on Cancer Center Support Grant (CCSG) Administrative Supplements as a successful mechanism to catalyze new areas of research. He highlighted some of the topics and research supported by the CCSG supplements, including HPV vaccination and Cancer Moonshot<sup>SM</sup> initiatives.

**One Least-Discussed, Least-Studied Challenge: Cannabis.** Dr. Croyle discussed what he considers to be an uncontrolled health experiment in the United States of America—the state-regulated cannabis program, highlighting the prevalence of the use of cannabis among youth. To examine cannabis use among cancer patients, the DCCPS awarded 12 CCSGs in FY 2020 to expand information on patterns of use, beliefs and attitudes, and perception of benefits and risks among patients with cancer. Ongoing survey data are being collected from a cohort of patients across a varied legal landscape. Preliminary results (unpublished data) suggest that 20–25 percent of all U.S. cancer patients may be using cannabis, representing a large uncontrolled exposure in this population. Dr. Croyle pointed out that the greatest challenge is U.S. Drug Enforcement Administration drug scheduling of controlled substances, and he proposed several strategies, including ramping up cannabis research.

**Health Disparities.** Dr. Croyle noted the significant expansion of the DCCPS research portfolio in health disparities and the fact that high-quality, state-of-the-art health disparities research is being funded. The Division is in its third generation of health disparities research, funding studies that are addressing the complexity and interaction of biological, environmental, behavioral, and socioeconomic factors in a sophisticated manner that will continue to inform the field. The CRCHD has heavily invested in the Division’s investigator training programs throughout the years, and RFAs and training efforts have resulted in a doubling of the health disparities research portfolio.

Discussing gaps and opportunities in the health disparities research portfolio, Dr. Croyle pointed out that research focused on American Indians/Alaskan Natives, a subpopulation with a tremendous cancer burden, is limited. Both cultural and tribal governance issues will need to be considered. He acknowledged Dr. Shobha Srinivasan, Senior Advisor for Health Disparities, DCCPS, who has devoted the last several years to outreach and collaboration with these communities. Other areas of limited research include sexual and gender minorities and geographic regions with persistent poverty. Dr. Croyle briefly noted collaboration opportunities and challenges, including revisiting the relationship among the American Cancer Society, CDC, and NCI, as well as international collaboration and data sharing under the European Union's General Data Protection Regulation.

**Transition to New Leadership.** Dr. Croyle acknowledged the DCCPS organizational leadership, remarking on the bright future of the Division under the direction of this team. He announced that the new DCCPS Director, Dr. Katrina A.B. Goddard, began her tenure in October 2021 and that the transition has been smooth.

### Questions and Answers

BSA and NCAB members expressed appreciation to Dr. Croyle for his leadership, for implementing critical administrative supplements where needed, and for his overall service to the NCI and NIH.

## IX. RFA/COOP. AGR., RFP, AND PAR CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF

### Office of the Director

#### Global Implementation Science for Equitable Cancer Control (GlobalISE Cancer Control) (New RFA/Coop. Agr.)—Dr. Gila Neta

Dr. Gila Neta, Program Director, DCCPS, presented a new RFA concept on global implementation science for equitable cancer control (GlobalISE Cancer Control). Global inequities in cancer control in reducing premature deaths are increasing. According to the *2020 WHO Report on Cancer*, progress is significantly slower in low-income countries. Many effective interventions across the cancer care continuum can prevent premature death from cancer, but progress has been slow, inconsistent, and incomplete. The NCI's goal to decrease the burden of cancer is to bridge this intervention implementation gap of underused, overused, and insufficient training, infrastructure, and governance to deliver an intervention. Understanding the barriers and testing strategies to overcome them are key to effective implementation science.

Dr. Neta emphasized that implementation science is identified as a priority area outlined in the *NCI Annual Plan & Budget Proposal for FY 2021*. To date, the NCI has funded 85 U.S.-based investigators, 12 of whom have conducted these studies from diverse geographical locations and are well positioned for future collaborations. These efforts are focused on U.S.-based cancer control, with limited initiatives in a region of great need, the low- and middle-income countries (LMICs).

The NCI proposes the GlobalISE Cancer Control program and a consortium to build LMIC-based implementation hubs using the U54 mechanism. Each award will support two investigator-initiated research projects and two cores: administrative and research capacity building. The consortium will address priority areas for the LMICs: focusing on adapting cancer control interventions, bundling services, integrating cancer control into primary care settings, and enhancing retention across the cancer continuum in otherwise fragmented systems. Nondomestic institutions will be eligible to apply. U.S.-based institutions must have an LMIC-based principal investigator or multiple principal investigators. U54 applicants should demonstrate a history of partnership, address high-priority

implementation gaps in cancer control, use appropriate approaches in their research design, and demonstrate institutional support for implementational science.

**Subcommittee Review.** 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 the Subcommittee’s enthusiasm and support for the concept. The Subcommittee appreciated the NCI staff responses to its requests for clarifications on the role of the NCI staff in the research, priority to build depth in implementation science, the eligibility, and success metrics. The Subcommittee further recommended that the NCI consider expanding the implementation science hubs to include other academic or research institutions based in LMICs as part of a future RFA.

The first-year cost for the one-time issuance is estimated at \$4 M for four U54 awards, with a total cost of \$20 M for 5 years.

### Questions and Answers

Dr. Earp commented that research capacity-building should be more of an interchange to develop trainees in the United States and in LMICs. Dr. Neta agreed with including a training component and pointed out that the DCCPS hosts the Training Institute for Dissemination and Implementation Research in Cancer (TIDIRC) and has instructed hundreds of investigators in cancer control, many of whom have global collaborations. She also noted that several of the Cancer Moonshot<sup>SM</sup>-funded Implementation Science Centers in Cancer Control (ISC3) also have global connections.

Dr. Chan asked how applications would be prioritized to fund the four centers, given that the response to the RFA could be robust. Dr. Satish Gopal, Director, CGH, explained that the aim is to support strong implementation science hubs that can address highly relevant contextual needs. He called attention to other related implementation science activities at the NCI, both domestic and international, including an open RFA for implementation science U01s focusing on populations infected with HIV. The start of this GlobalISE Cancer Control program with four centers, Dr. Gopal emphasized, will be a group that the NCI can effectively coordinate and leverage with other implementation science activities, including the training activities through TIDIRC.

**Motion.** A motion to approve the Office of the Director’s (OD) new RFA/Coop. Agr. entitled “Global Implementation Science for Equitable Cancer Control (GlobalISE Cancer Control)” was approved unanimously.

### Division of Cancer Prevention

#### **PREVENT Cancer Preclinical Drug Development Program (Re-issue RFP) —Dr. Shizuko Sei**

Dr. Shizuko Sei, Medical Officer, Chemopreventive Agent Development Research Group, Division of Cancer Prevention (DCP), presented a re-issue RFP concept for the PREVENT Cancer Preclinical Drug Development Program (or PREVENT). The mission is to support extramural investigators through preclinical development of innovative cancer preventive or interceptive agents and biomarkers, with the goal of clinical translation. PREVENT applications are peer reviewed and ranked by the Scientific Review Panel (outside members), followed by the final selection by the Management and Administration Committee (MAC) composed of expert scientists from DCP and other Divisions within the NIH. After approval, project strategies are developed in consultation with the applicants, implemented through contracts (not grants), and managed according to milestones following go/no-go decision criteria. The current scientific focus of PREVENT is the development of novel molecularly targeted agents or immunopreventive agents (e.g., cancer vaccines) and response-predictive biomarkers.

Established in 2011, PREVENT had the goals and priorities of chemoprevention agent development using organ-specific carcinogenesis models. During the last 10 years, the program has transformed, with the preclinical development pipeline retaining the scientific focus, but with an increased emphasis on clinical translation. Dr. Sei noted several guiding principles for the preclinical pipeline, including clearly defining target cohorts, validating targets and pathways in the oncogenic process, minimizing safety concerns to obtain the maximum benefit-to-harm ratio, and dropping failing projects early by utilizing go/no-go decisions made at key project milestones. Regarding transformational impact, PREVENT has been driven not only by emerging science in premalignant biology or tumor immunology, but also by the lessons learned from terminated projects related to the models, targets, and study cohorts used.

The DCP drug development program models the NCI Experimental Therapeutics (NExT) Program and consists of three critical components, preclinical toxicology studies, early-phase clinical trials, and Phase III efficacy trials, which are supported by programs within DCP. PREVENT serves as the preclinical development engine to advance candidate agents to other programs. The DCP received BSA approval in March 2021 to establish the Cancer Prevention-Interception Targeted Agent Discovery Program (CAP-IT). PREVENT expects to support drug development needs emerging from CAP-IT.

PREVENT implements projects utilizing the NCI network of contract companies, competitively selected based on their expertise and resources. The primary contractors can solicit the services of subcontractors to augment technical support as needed. Approved concepts can enter the PREVENT pipeline at the proof-of-concept, secondary testing, or advanced preclinical development stages. Each project advances through the pipeline with go/no-go decisions made at key milestones with the oversight and approval of the MAC. The DCP Cancer Prevention Clinical Trials Network (CP-CTNet) and External Steering Panel (outside members) make the final go/no-go decision for agents successfully advancing to the clinical development team.

To date, PREVENT has received 390 applications, of which 101 have been approved, resulting in 115 contract projects. Of the 115 projects, 63 entered the pipeline as proof-of-concept, 33 at secondary testing, and 19 at advanced preclinical development. The distribution of the 115 projects spans chemoprevention, immunoprevention, and biomarker developments; 74 have been completed or closed, 27 received a go decision, and 7 advanced to clinical trials. Dr. Sei explained that most of the no-go decisions occurred in the proof-of-concept stage of the pipeline, demonstrating PREVENT's ability to drop failing projects early, without undue expense. PREVENT-supported agents (e.g., aerosolized bexarotene) advancing to clinical development utilize organ-targeted agent delivery to minimize systemic toxicity while achieving local cancer prevention, an approach unique to this program.

This re-issuance will continue the unique efforts of PREVENT to support cancer preventive agent research and development, with emphasis on clinical translation. The RFP will enable PREVENT to support the increasing demands for quality control in pharmaceutical manufacturing practices and increasing the number of contract projects to accommodate other DCP programs.

**Subcommittee Review.** Dr. Flaherty expressed the Subcommittee's support for the concept, which addresses an area of unmet need. Dr. Flaherty noted that PREVENT focuses on cancer agent research and development that is not being addressed in the private sector. The Subcommittee highlighted that the past performance and productivity of PREVENT has been exceptional, the program has been successful in supporting a broad spectrum of contracts, and it has been strategic to embed the go/no-go criteria at each state of the drug development pipeline.

The first-year cost for the one-time re-issuance is estimated at \$13 M in years 1 and 2, \$15 M in year 3, and \$17 M in years 4 and 5, with a total cost of \$75 M for 5 years.

## Questions and Answers

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology, Professor Emeritus in Neurosurgery, Duke University Medical Center, asked whether agents that prevent low-grade tumors from progressing to high-grade tumors were supported. Dr. Sei confirmed that the DCP's purview included cancer preventive and intercept agents, although this specific presentation did focus on both types.

**Motion.** A motion to concur on the re-issuance of the DCP's RFP entitled "PREVENT Cancer Preclinical Drug Development Program" was approved unanimously.

### Division of Cancer Control and Population Sciences

#### **Cancer Epidemiology Cohorts: Research Opportunities in Established Studies (New PAR)— Dr. Joanne Elena**

Dr. Joanne Watters Elena, Program Director, DCCPS, presented a new PAR concept on cancer epidemiology cohorts for established studies. The purpose is to provide continued support for established cohort studies that address novel, innovative research questions across the cancer control continuum. Established cohort studies are defined as those studies that have achieved their initial, planned recruitment goal.

This PAR will replace PAR 20-294 (Cohort Infrastructure for Cancer Epidemiology Cohorts) due to expire in November 2022 but also will focus on hypothesis-based research. This concept aligns with the recommendations of the NCAB *ad hoc* Working Group on Strategic Approaches and Opportunities in Population Science, Epidemiology, and Disparities, emphasizing the need to continue to provide sufficient infrastructure support for cohorts to conduct or facilitate research that addresses critical scientific gaps.

Dr. Elena noted that cohort studies advance knowledge. In fact, prospective cohort studies have identified environmental, behavioral, and genomic factors associated with cancer incidence, morbidity, and mortality. These studies had informed interventions and guidelines to prevent or mitigate the effects of cancer and its treatment. In addition, cohort studies are a rich resource of data and biospecimen collections from diverse populations. The NCI proposes that requiring scientific aims with specific research questions is one mechanism designed to support established cancer epidemiology cohorts. This approach is anticipated to guide scientific design, ensure use of appropriate methods, and bring the field closer the ultimate goal of advancing scientific knowledge and the health of the population.

For this PAR concept, applicants must address key scientific gaps, include hypothesis-based research questions in their aims, and have core infrastructure support. Priority will be given to novel research that includes understudied populations and directly informs future interventions, guidelines, and/or clinical management strategies. Dr. Elena emphasized that this concept does not support initiating new cohorts.

A portfolio analysis identified 31 DCCPS-supported cancer epidemiology cohorts. The distribution approximates the U.S. population for White/Caucasian, Black/African American, and Asian American groups, but not the Hispanic population.

**Subcommittee Review.** Dr. Leslie L. Robison, Chairman, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Associate Director, St. Jude Comprehensive Cancer Center, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Robison stated that the Subcommittee appreciated the NCI staff responses to its requests for clarification on transitioning cohorts from the PAR-20-294, RFP non-responsive criteria, and depth of the DCCPS portfolio.

**Motion.** A motion to approve the DCCPS' new PAR entitled "Cancer Epidemiology Cohorts: Research Opportunities in Established Studies" was approved unanimously.

### **Division of Cancer Control and Population Sciences**

#### **Cancer Epidemiology Cohorts: Building the Next Generation of Research Cohorts (Clinical Trials Not Allowed) (New PAR)—Dr. Tram Kim Lam**

Dr. Tram Kim Lam, Program Director, DCCPS, presented a new PAR on building the next generation of cancer epidemiology research cohorts. The purpose is to support initiating and building the next generation of population-based cancer epidemiology cohorts to address specific knowledge gaps in cancer etiology and survivorship. These cohorts will allow investigations of new and unique exposures and expand the diversity of populations, including, but not limited to, race and ethnicity.

In terms of the rationale for new cohorts, Dr. Lam explained that the changing environmental and demographic landscape of the United States will affect cancer-related burden and have significant implications on cancer control and prevention in the future. The U.S. population is becoming more multiracial and notably more diverse than in the past decade. Within this diverse population of Americans, many are not well represented in biomedical research. In the context of a changing landscape, unique and new exposures are not well understood regarding their influence on cancer risk and survivorship. Next-generation research cohorts should be able to address current research gaps, enable prospective investigation of new scientific questions, and foster incorporation and adaptation of new technologies and approaches.

The NCI proposes this concept as a pragmatic approach to meet the challenges of the future and establish the foundation for a forward-looking research agenda. This PAR will support the methodological work necessary to initiate and build next-generation cancer epidemiology cohorts. Applicants must address key scientific and resource gaps and propose concrete methodological work and community engagement. Dr. Lam emphasized this concept is not responsive to proposals addressing established cohorts.

Of the 31 DCCPS-supported cancer epidemiology cohorts, 75 percent of the representations of Asian American and Hispanic populations are contributed by the Multiethnic Cohort. The median age of several of the established and well-known etiology cohorts, such as Nurses' Health Study, Health Professional Follow-up Study, and the Multiethnic Cohorts, is 75 years or older.

**Subcommittee Review.** Dr. Ian M. Thompson, Jr., President, CHRISTUS Santa Rosa Medical Center Hospital, Texas Urology Group, expressed the Subcommittee's strong enthusiasm and support for the concept. Dr. Thompson commended the NCI for establishing prior cohorts that have provided insight into a broad range of related to carcinogenesis and environmental exposures. The Subcommittee agreed that the concept should test new methods to accrue difficult-to-enroll populations that have not previously been enrolled in trials and to have milestones for the projects.

### **Questions and Answers**

Dr. Lam clarified that the scientific gaps would drive the appropriateness of the study populations, which is not limited to population-based cohorts.

In response to a question from Dr. Chan about use of intermediate biomarkers as endpoints, Dr. Lam noted that short-term research studies that will be supported by this concept will allow assessment of short-term research questions, including biomarkers of carcinogenesis.

**Motion.** A motion to approve DCCPS' new PAR entitled "Cancer Epidemiology Cohorts: Building the Next Generation of Research Cohorts (Clinical Trials Not Allowed)" was approved unanimously.

### **Division of Cancer Control and Population Sciences**

#### **Cancer Control Research in Persistent Poverty Areas (New RFA/Coop. Agr.)— Dr. Shobha Srinivasan**

Dr. Srinivasan presented a new RFA concept on cancer control research in persistent poverty areas. As defined by the U.S. Department of Agriculture (USDA), persistent poverty areas are counties where 20 percent or more of the population has had an income below the federal poverty line for the last 30 years, thus capturing generational poverty and structural institutional problems in these areas. DCCPS investigators reported in the 29 October 2020 issue of *Cancer Epidemiology, Biomarkers, and Prevention* that people living in persistent poverty areas have higher cancer mortality than those in other counties. The study also revealed a heightened risk for mortality in persistent poverty counties for screenable and preventable cancers.

Dr. Srinivasan noted that for this RFA, the NCI worked with the USDA to refine the definition of persistent poverty from the county level to the census-tract level to be more inclusive of smaller areas of extreme poverty. This new definition allows broader representation across all states and increases the count of the total population of those living in persistent poverty by nearly 75 percent. Unique to persistent poverty areas and populations is a lack of adequate housing and greater environmental degradation. These populations also have very high rates of obesity, smoking, HPV infection, sun exposure, and food insecurity. The education levels tend to be lower, unemployment higher, and access to health care inadequate.

The NCI is proposing this concept to conduct cancer control and prevention research in partnership with communities and clinics in persistent poverty areas. This research will support developing data integration and sharing processes, conducting multilevel and multifactorial interventions, and implementing training of transdisciplinary teams for junior investigators. The RFA will support establishing U54 specialized centers, with administrative and research/data infrastructure, and investigator support cores. Each center will conduct a minimum of two research and two pilot projects. Studies will be restricted to the provided list of census tracts; focus on community, institutional, and structural levels; and be multilevel and multifactorial.

An NIH portfolio analysis examining funded grants during the last 10 years identified only five projects that focused on people living in persistent poverty areas. CCSGs Administrative Supplements issued in March 2021 to expand research in persistent poverty areas resulted in only five funded projects. A notice of special interest released during the summer of 2021 soliciting applications focusing on expanding research in poverty persistent areas through project research programs is accepting applications, but so far has not received any.

**Subcommittee Review.** Dr. Michelle M. Le Beau, Arthur and Marian Edelstein Professor of Medicine, Director, University of Chicago Comprehensive Cancer Center, The University of Chicago, expressed the Subcommittee's enthusiasm and support for the concept, which is timely and addresses a high unmet need. Observing the limited research in this area in the NIH and NCI portfolios and to implement interventions, the Subcommittee recognized that it would require better understanding of the interrelated and synergistic effects of persistent poverty and other socioeconomic health factors at the structural and institutional levels. Dr. Le Beau noted several strengths of the concept: using the census tracts to define persistent poverty areas, addressing sustainably through community partnerships, and establishing a network of researchers.



The first-year cost for the one-time issuance is estimated at \$10 M for four U01 U54 awards, with a total cost of \$50 M for 5 years.

### **Questions and Answers**

When queried as to whether Cancer Centers that do not accept Medicaid were excluded from participating, Dr. Srinivasan clarified that not accepting Medicare was not a criterion for exclusion from participating in the RFA. The NCI encourages CCSG investigators to engage in this area of research and seek partnerships.

In response to a query regarding the availability of the census-tract list for the RFA if it is essential that investigators be aware of those areas and build partnerships prior to the funding announcement, Dr. Srinivasan stated that the list generated by the USDA will be made available in January or February 2022.

**Motion.** A motion to approve the DCCPS' new RFA/Coop. Agr. entitled "Cancer Control Research in Persistent Poverty Areas" was approved unanimously.

### **THURSDAY, 9 DECEMBER 2021**

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

Dr. Carpten called Members to order on the final day of the 5<sup>th</sup> Virtual Joint Board Meeting of the BSA and NCAB and welcomed members of the Board, *ex officio* members, President's Cancer Panel members, liaison representatives, staff, and guests.

#### **XI. DIVISION OF CANCER PREVENTION: VISION—DR. PHILIP E. CASTLE**

Dr. Philip E. Castle, Director, DCP, presented an overview of the Division and its vision for the future. He explained that trends in cancer deaths have declined since 1975, but further progress is needed in reducing the incidence of cancer. About \$200 B is spent on cancer care every year, of which about 10 percent reflects patients' out-of-pocket expenses. Dr. Castle presented the DCP's new mission statement. He highlighted the DCP leadership and noted its 10 branches. The DCP works in three areas: preventive agents; biomarkers for screening and early detection; and symptom science, prevention, and management. The DCP is engaging extramural researchers and community stakeholders in discussions (e.g., in workshops and symposiums) regarding the Division's forward direction. Recent efforts have included engagement with industry partners.

Tools for cancer prevention include primary (e.g., avoidance, vaccination) and secondary (e.g., screening, treatment/interception) measures. Dr. Castle stated that more work in the area of cancer interception is needed. He framed DCP's work in terms of a pipeline across the translational research continuum that involves programs in the areas of basic science research, translation to humans, translation to patients, translation to practice, and translation to community. Dr. Castle underscored the value of the PREVENT Program and acknowledged Drs. Shizuko Sei and Robert Shoemaker for their leadership in this effort. He noted that the CP-CTNet is led by Dr. Eva Szabo and includes administrative offices across the United States. He briefly outlined examples of recent and upcoming protocols in the CP-CTNet.

Screening and early detection is an important component of the Division, and risk-informed screening has become a central focus. Presently, screening options are limited to breast, cervix, colorectal, lung, hepatitis C virus, and prostate in select populations. More work in this area is needed. Dr. Castle outlined the screening and early detection research and development pipeline. He highlighted the Early Detection Research Network (EDRN), which involves 350 associate members focusing on conditions

related to prostate and urologic systems, breast and other gynecologic systems, lung and upper systems, the digestive system, and colon and other gastrointestinal systems.

The NCI Community Oncology Research Program (NCORP) is a national and international program focused on cancer prevention, control, and oncology that now includes more than 1,000 clinical sites through 46 centers and affiliates, as well as more than 4,000 investigators. Dr. Castle briefly outlined design modifications to the Tomosynthesis Mammographic Imaging Screening Trial (TMIST) and presented the updated accrual. NCORP activities include large screening and management trials (e.g., TMIST, Five- or Ten-Year Colonoscopy for 1–2 Non-Advanced Adenomatous Polyps [FORTE]), symptom management and quality-of-life trials (e.g., Immune Checkpoint Inhibitor Toxicity [I-CHECKIT], Optimizing Functional Outcomes of Older Cancer Survivors After Chemotherapy), and other studies (e.g., comparing the clinical impact on pancreatic cysts of low- versus high-intensity surveillance, comparing the non-inferiority of salpingectomy to salpingo-oophorectomy to reduce the risk of ovarian cancer among BRCA1 carriers).

Liquid biopsy (i.e., multi-cancer early detection in the prevention space) has gained recent interest, and the Trans-NCI Liquid Biopsy/Multi-Cancer Early Detection Program involves representatives from the Centers for Medicare & Medicaid Services (CMS) and FDA. Dr. Castle listed outcomes of the Multi-Cancer Early Detection (MCED) Study Design Workshop: Current knowledge on MCED assays focuses on diagnostic performance, specificity appears to be high (i.e., 97% or higher), and MCED tests present novel implementation challenges. Several themes emerged from the workshop: The NCI should support a trial to evaluate MCED assays, and several unknowns are present (e.g., variability in diagnostic workup, the need to assess the full process for the workup and when to stop the workup) for the screening process. Additional themes from the workshop included ensuring enrollment of various populations (e.g., underserved, diverse, vulnerable, high-risk), the need for a concrete recruitment process, and the need for adequate follow-up.

Dr. Castle proposed that precision cancer prevention is a crowning achievement based on biomarker and preventive agent pipelines to detect and mitigate cancer risk. He presented a pipeline for symptom science and management; several RFA and PAR considerations have been published to support early discovery and translation to humans. NCORP is central to this effort, and the Cancer Moonshot<sup>SM</sup> consortium addressing tolerability is focused on defining endpoints. Symptom management and toxicity mitigation involve the following efforts: understanding mechanisms of action for the chronic adverse effects, rigorously characterizing the clinical syndrome for the toxicity or symptom, and capturing how the patient functions and feels through patient-reported outcomes.

NCI-wide research opportunities are as follows: molecular and cellular mechanisms that underlie the development of cancer therapy, induced severe adverse sequelae, clinical characterization of cancer therapy, induced adverse sequelae and mechanism-based interventional strategies, and analyzing and interpreting clinician and patient adverse event data to better understand tolerability. Dr. Castle also highlighted the Cannabis, Cannabinoids, and Cancer Workshop, which was convened jointly by several NCI Divisions, the National Institute on Drug Abuse, and the FDA. The workshop monograph was published in the *Journal of the National Cancer Institute Monographs* in early December.

Dr. Castle concluded by outlining proposed DCP priorities: biological and population risk-informed interventions (e.g., precision cancer prevention, harmonizing care), obesity (e.g., understanding how obesity contributes to carcinogenesis), and symptom science/precision symptom prevention and management (e.g., understanding the “etiology” of symptoms, explaining adverse responses to treatments, and moving symptom management from trial-and-error treatment to precision medicine). Dr. Castle proposed the use of new technologies, self-collection, and point-of-care testing to bring a higher standard of care to underserved populations who typically are at higher risk of cancer. Investments in staffing and knowledge are necessary for further advancement in this area. Immunology and preventive vaccination

also represent an area for further work. Dr. Castle emphasized the importance of redefining precision cancer prevention to promote health equity.

### **Questions and Answers**

NCAB Chair Dr. Carpten asked about integration of risk assessment across DCP programs. Dr. Castle responded that emerging data have expanded capabilities for polygenic risk score, particularly in the screening context for prostate and breast cancer. Members were informed that polygenic risk score can be applied across the entire care continuum. Additionally, many institutions have their own risk score calculators, which have not been validated. The importance of communication regarding risk was emphasized.

Dr. Le Beau inquired about additional tests beyond DNA and RNA (e.g., protein, liquid biopsies, breath, urine). She also asked about structuring clinical trials to ensure sufficient participation by underrepresented populations. Dr. Castle responded that infrastructure is in place to ensure true representation, but biomarkers for tests could have been informed by previous collections in which systematic bias was present. He also informed Members that the Liquid Biopsy Consortium is pursuing efforts related to additional tests; he noted the importance of obtaining sufficient data that warrant inclusion in the trial.

Dr. Chan asked about embedding studies within existing clinical trials (e.g., trials of early detection markers). Dr. Castle stated that most trials include a biomarker component. Because trials are observational, interpretations are challenging. Dr. Castle added that he intends to discuss surrogate endpoints at an upcoming Cancer Research UK workshop. He added that collection of biospecimens provides valuable insight.

Dr. Andrea A. Hayes-Jordan, Byah Thompson Doxey Distinguished Professor of Surgery, Division Chief, Pediatric Surgery, Surgeon-in-Chief, University of North Carolina Children's Hospital, expressed concern about specimen processing in low-resource communities. Dr. Castle agreed that broad implementation of these technologies is a concern. He added that he looks forward to engaging with DCCPS on this topic.

Dr. Mustian inquired about the potential use of clinical trial planning grants (R34s) to prepare for large supportive care clinical trials. She also asked about resourcing and providing additional support to NCORP sites to encourage enrolling more underrepresented minorities in clinical trials. Dr. Castle agreed that representation and resources both reflect ongoing challenges. Dr. Sharpless suggested an update on underrepresented minority accrual in the NCORP trials.

## **XII. ACHIEVING HEALTH EQUITY THROUGH PREVENTION AND IMPLEMENTATION SCIENCE OF PATIENT NAVIGATION IN UNDERSERVED POPULATIONS— DR. MELISSA A. SIMON**

Dr. Melissa A. Simon, Vice Chair of Research, George H. Gardner Professor of Clinical Gynecology, Professor, Departments of Obstetrics and Gynecology, Preventive Medicine and Medical Social Sciences, Associate Director, Community Outreach and Engagement, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, discussed the role of research and clinical infrastructure design in achieving health equity in the United States. To embed equity in cancer care delivery and improve outcomes across diverse populations, implementation science approaches must be applied to involve relevant stakeholders in all related processes and structures.

Dr. Simon defined inequality (unequal access to opportunities), equality (evenly distributed tools and assistance), equity (custom tools that identify and address inequalities), and justice (fixing the system to offer equal access to health tools and opportunities)—terms commonly used in the patient navigation

and implementation science fields. Dr. Simon noted that systemic racism drives structural inequities that affect social determinants of health, a challenge that must be tackled by community-driven solutions and programs like patient navigation assistance. She added that structural inequities and structural racism can influence the entire research pipeline, including funders and funding opportunities, scientists, study protocols, study participants, and the dissemination of research findings.

Dr. Simon provided several examples of U.S. Preventive Services Task Force (USPSTF) recommendations that were updated to better address the needs of minority populations that included lowering the recommended age for colon cancer screening to age 45 and reducing the recommended cigarette pack-year history for lung cancer screening. Dr. Simon explained the Consolidated Framework for Implementation Research (CFIR), one of several implementation frameworks for practical evidence-based interventions. CFIR is a hybrid design in which interventions and their implementation processes are being investigated. Dr. Simon reiterated that systemic racism potentially could affect each realm of these structures (e.g., society and sociopolitical structures, organizational culture within a particular health center or health care delivery team, patient experiences of discrimination or distrust).

Dr. Simon discussed her work investigating and applying implementation science to women's health equity in Chicago. She noted that disparities in breast cancer mortality rates between Black and White patients have increased throughout the past several decades. Whereas this difference was negligible in the early 1980s, in 2006, breast cancer mortality rates in Black women were 62 percent higher than in White women. To narrow this gap, an environmental scan to identify barriers to effective treatment was conducted across 27 clinics by systems engineers from the Kellogg School of Management at Northwestern University. Patient navigation and policy advocacy efforts were then implemented at these sites to mitigate intrapersonal barriers (e.g., insufficient health-seeking behavior, fear and mistrust, lack of knowledge), community barriers (e.g., social norms, including mistrust of health care system), health system barriers (e.g., variation in access to and quality of breast health resources), and public policy barriers (e.g., insufficient funding for state screening programs for underserved women).

Patient navigation is not a "one size fits all" effort; intervention strategies must be patient-centered, community-centered, evidence-based, and embedded with anti-racism approaches. Dr. Simon presented an example of a health care sequence checklist that was used to improve breast cancer patient care. A printed copy of the checklist, which included timelines for various care options, options for future care, and contact numbers for relevant care providers, was given to patients, caregivers, the patient care team, and navigators to improve communication and consistency during the care process. Another example of improved patient navigation was the DuPage Patient Navigation Collaborative, which is assisting in building relationships among community organizations, health care providers, and local health departments. Dr. Simon noted that through these efforts, the breast cancer mortality gap between Black and White women was reduced to 36 percent in 2017. She added that these numbers can still be improved and expressed appreciation of the NCI for funding these initiatives through the Chicago Cancer Health Equity Collaborative (CCHEC).

Dr. Simon highlighted several recent efforts to improve research, community collaboration, and diverse workforce development in Chicago, including Health for All, a tool created via a partnership among Chicago Public Libraries, Northwestern University, and the Chicago Department of Health that was founded to help people make informed decisions about clinical trial participation.

In closing, Dr. Simon listed key points in advancing equity to improve cancer outcomes for everyone in the United States, including optimized training, mentorship, and career development pathways; enhanced diversity, equity, and inclusion (DEI) to improve community engagements and support; and structured collaborative research opportunities. She expressed appreciation for NIH efforts to improve scientific diversity through the NIH initiative on ending structural racism, UNITE, and for including a DEI component in the CCSGs.

## Questions and Answers

NCAB Chair Dr. Carpten noted that the “Financial” section of the non-navigator-based patient form merely instructed patients to refer to their case workers and asked for further discussion on this aspect of an intervention. Dr. Simon explained that the example she provided was one version of the form. She agreed that many financial barriers to equitable health outcomes exist and added that patient navigators help address financial issues by connecting people with available resources.

Dr. Ideker asked whether complex factors influencing disparate health outcomes must be deconvoluted before being addressed. Dr. Simon pointed out that implementation science must be informed by an understanding of systemic factors and local histories of systemic racism but added that those disparities need not be detailed in full. She noted that health inequalities in Chicago map directly onto boundaries demarcated by historical discriminatory redlining practices and that evidence-based interventions must be scaled to address these discrepancies.

### **XIII. IMPLEMENTING PROGRAM-BASED INTERVENTIONS TO IMPROVE POPULATION-LEVEL LUNG CANCER OUTCOMES: THE MID-SOUTH MIRACLE—DR. RAYMOND U. OSAROGIAGBON**

Dr. Raymond U. Osarogiagbon, Chief Scientist, Baptist Memorial Health Care Corporation (BMHCC), discussed program-based interventions in the context of BMHCC and the geography of lung cancer in the United States, the population impact pyramid and the “Mid-South Miracle,” implementation of effective interventions, and quantifying population-level impact. The incidence and mortality of lung cancer has declined sequentially, but these trends are not uniform across the United States. Disparate regions are concentrated in the southern and midwestern regions of the United States; these clusters reflect higher smoking rates.

The BMHCC is a not-for-profit health care system deployed in Arkansas, Mississippi, and Tennessee. The service area also includes parts of Alabama, Kentucky, and Missouri—states with some of the highest per capita lung cancer mortality statistics. The BMHCC manages 1,200 to 1,300 lung cancer cases each year.

Assessment of population impact provides insight on the use of resources for maximum benefit. These efforts include tobacco control, management of incidental lung nodules, low-dose computed tomography (CT) screening, treatment selection, optimal surgical resection, optimal pathologic evaluation, and optimal systemic therapy. Dr. Osarogiagbon explained that these seven programs will be deployed vertically (i.e., in metropolitan Memphis) and horizontally (i.e., across the health care system). The three-tiered approach involves population science, team science, and implementation science.

Low-dose CT screening is challenging to implement, and many eligible patients are unable to obtain a screening test. Several of the regions with high per capita mortality (e.g., Alabama, Arkansas, Mississippi, Tennessee, West Virginia) report low screening rates. The challenge is to determine other approaches for detection, such as algorithmic management of incidentally detected lung nodules. Dr. Osarogiagbon presented data demonstrating the effectiveness of the nodule program, compared to screening.

Dr. Osarogiagbon noted that racial disparities related to lung cancer detection are present; Black individuals represented 16 percent of the screened patients with lung cancer but 27 percent of patients in the nodule program with lung cancer, which is similar to the health care system as a whole. Additionally, 13 percent of those diagnosed with lung cancer in the nodule program are people who never smoked and therefore would have been ineligible for screening. Furthermore, the median quit duration for the lung cancer patients in the nodule program is 16 years, meaning that more than half of these patients would not have been eligible for screening because they quit smoking too long ago. The programs have been

disseminated across multiple sites in the health care system. These efforts have enabled an increase in detection volumes, particularly through the nodule program.

Dr. Osarogiagbon explained that the next challenge is to provide curative treatment to the identified patients. He explained that many patients with early-stage lung cancer do not receive the treatment that they need (e.g., surgical resection). Disparities in proper treatment selection are present among geographic regions, particularly at the county level. Dr. Osarogiagbon outlined data related to this topic, explaining that interdisciplinary care decision making provides better odds of the appropriate treatment's being implemented and subsequently, improved odds of survival. Now, the challenge is to implement this approach across the health care system. Dr. Osarogiagbon also noted interventions regarding the use of a lymph node kit to improve the compliance rates (i.e., in line with the National Comprehensive Cancer Network standards) for surgical resection.

### **Questions and Answers**

Dr. Otis W. Brawley Bloomberg Distinguished Professor of Oncology and Epidemiology, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, commented that some hospitals now are offering spiral-CT screening in the lung but are not equipped with capabilities to perform appropriate procedures and refer patients to other centers. Dr. Osarogiagbon emphasized the importance of developing infrastructure to group patients into pathways of care. He pointed to the importance of team and implementation science, as well as engagement and human resources. In a follow-up comment, Dr. Brawley stated that lung cancer screening was shown to reduce the risk of death by 20 percent and that for every 5.4 lives saved, 1 person died during biopsy and work-up of abnormal findings.

Dr. Margaret R. Spitz, Professor, Department of Medicine, Dan L. Duncan Cancer Center, Baylor College of Medicine, asked for clarification on the three groups—screening, nodule, and multidisciplinary—that were presented. Dr. Osarogiagbon clarified that the nodule group represents patients who were tested in a radiologic study (e.g., following injury from a car accident), during which time potential areas of concern were detected. The nodule program collects data on radiology reports using keywords, and a team of navigators use the Fleischner Society guidelines to triage patients into different risk categories, with ongoing surveillance for patients in the high-risk group. Dr. Spitz asked whether the patients seen in the clinic were symptomatic. Dr. Osarogiagbon responded that the multidisciplinary cohort was used to contextualize early detection; many had been diagnosed with lung cancer previously.

## **XIV. RFA/COOP. AGR. AND PAR CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF**

### **Division of Cancer Treatment and Diagnosis/Division of Cancer Biology**

#### **Pediatric Immunotherapy Network (PIN) (New RFA/Coop. Agr.)—Dr. Anju Singh**

Dr. Anju Singh, Program Director, Division of Cancer Treatment and Diagnosis (DCTD), presented a new RFA concept to establish a Pediatric Immunotherapy Network (PIN). Pediatric cancer and immunotherapy strategies are distinct from those for adults. Most immunotherapies that are successful in treating children with cancer rely on synthetic immunity. Of the successful therapies, only the ganglioside monoclonal antibody, GD2, is indicated for treating a solid tumor. Pediatric solid tumors remain an area of unmet clinical need, but challenges exist related to studying these tumors. Because pediatric solid and brain tumors are rare, both the number of patients with any given tumor and specimens of that tumor are limited. The role of the developing immune system in this class of tumors is relatively unknown. The tumor microenvironment is not well understood, the tumor mutation rate is low, and the

risk of therapy-related toxicities is increased, including neurotoxicity for the developing brain. Last, appropriate model systems that consider tumor heterogeneity and known targets are lacking.

An NCI portfolio analysis of studies examining pediatric solid tumor immunotherapy revealed only 31 grants, suggesting a need to increase this research, both preclinical and clinical. The NCI published a request for information (RFI) in June 2021 seeking input from the research community on the gaps and opportunities in advancing pediatric immunotherapy. Responders identified several topics to advance, including targetable antigenic epitopes; binders and immunotherapy agents; and pediatric preclinical models, especially for brain tumors. The RFI responses have informed the development of this concept.

The NCI is proposing to establish a network dedicated to pediatric immunotherapy, a Pediatric Immunotherapy Network (PIN), to develop translatable novel immunotherapy approaches for children and adolescents with solid tumors, including brain tumors, aiming toward eventually clinical applications. The PIN will focus on basic research to a clinical trial and reverse translational studies. This RFA will support a network of Research Project-Cooperative Agreements (U01) sites, with administration coordinated by an individual U01 and the NCI. The PIN will interact with existing NCI pediatric cancer networks and resources, such as the CCDI and COG, and will build on the accomplishments of the Cancer Moonshot<sup>SM</sup>-funded PI-DDN. This RFA will be responsive, for example, to proposals aiming to develop novel pediatric tumor-associated antigens or conduct reverse translation studies using clinical specimens. Dr. Singh noted that PIN investigators can apply to the NExT Program.

**Subcommittee Review.** Dr. Robert H. Vonderheide, John H. Glick, MD Abramson Cancer Center's Professor, Professor of Medicine, Perelman School of Medicine, Director, Abramson Cancer Center, University of Pennsylvania, expressed the Subcommittee's support for the concept. Dr. Vonderheide remarked that the concept is addressing a different biology with scientific considerations that are limited in the NCI portfolio and leverages the Cancer Moonshot<sup>SM</sup> programs. The Subcommittee pointed out the unmet need being addressed—immunotherapy strategies for pediatric populations—and is using a model that has worked well for the NCI, a network of U01s.

The first-year cost for the one-time issuance is estimated at \$6 M for six to eight U01 awards, with a total cost of \$30 M for 5 years.

## Questions and Answers

Dr. Hayes-Jordan highlighted that significant work is needed to establish an appropriate and representative funding line for immunotherapies for pediatric populations and hopes that the U01 network would encourage or inspire new investigators and young investigators to engage in this opportunity.

Dr. Baker asked whether a specific selection of the complementary projects was represented in the cluster of U01s, or whether the RFA would select the strongest U01s. She also asked about particular themes that would be addressed by the different U01s and how a coordinating center will actively facilitate exchange of reagents, particularly model systems critical for proper studies to be conducted across different groups. Dr. Singh explained that the applications must be meritorious and will undergo a thorough review process. The reviewers will consider the gaps in the current NCI portfolio of this research, which will inform the funding plan. NCI staff and the Network's steering committee (composed of the U01 investigators) will provide administrative coordination and will facilitate access to resources.

NCAB Chair Dr. Carpten inquired about the integration of current knowledge about the biology and immunotherapies in the adult populations. Dr. Singh noted that such an integration had not been considered for the PIN and called attention to similar efforts being planned within other NCI programs and initiatives, including the IOTN, PI-DDN, and Pre-medical Cancer Immunotherapy Network for Canine Trials (PRECINCT). Dr. Sharpless added that differences between childhood and adult cancers

are more straightforward for developing therapies consisting of small molecules and antibodies, but more challenging for cellular immunotherapy. He underscored that coordination between adult and pediatric cellular immunotherapies has been particularly successful and remains a topic of interest to the NCI.

**Motion.** A motion to approve the DCTD's/Division of Cancer Biology's (DCB) new RFA/Coop. Agr. entitled "Pediatric Immunotherapy Network (PIN)" was approved unanimously.

### **Division of Cancer Biology/Office of the Director**

#### **Integrating Health Disparities into Immuno-Oncology Research (HDIO) (New RFA)— Dr. Lillian Kuo**

Dr. Lillian Kuo, Program Director, DCB, NCI, presented a new RFA concept on integrating health disparities into immuno-oncology research (HDIO), which is a joint DCB and CRCHD program. Dr. Kuo pointed out the scientific gaps to integrating health disparities into immuno-oncology research. Multilayered impediments in access to care, interdisciplinary research, and implementation science need to be directly addressed in the immuno-oncology research ecosystem, and complementary basic science research is needed.

The basic science challenges in cancer health disparities research remain the complex and overlapping biological and immunological factors affecting the disparity and difficulty in accessing sufficiently powered or well-curated specimens, particularly due to the lower numbers of underrepresented groups recruited to clinical trials. Although the research gaps are multifaceted, this basic science concept's objective is to integrate health disparities throughout the NCI immuno-oncology research continuum. Research gaps at the intersection of health disparities in immuno-oncology include understanding inflammatory metabolic immune profiles of immunotherapy treatment and response across underrepresented populations and investigating genetic immune signatures, immune infiltrates, and distinct tumor-immune microenvironments that may contribute to cancer health disparities.

A portfolio analysis of NCI P01s (multidisciplinary projects) addressing health disparities and immunotherapy from FY 2017 to the present revealed a potential applicant pool for studying health disparities in immuno-oncology, but a sparsity of multidisciplinary projects that incorporate health disparities research. The DCB recognizes that addressing this unmet need will require a multipronged programmatic approach to integrate health disparities into immuno-oncology research. Two options are to leverage ongoing basic and translational research projects supported through the NCI and to support feasibility and planning projects to strengthen studies for P01s.

This RFA has the goal of building a cohort of immuno-oncology research P01s with integrated health disparities research and will utilize feasibility and planning studies (P20s) to build collaborations, appropriate sample sets, and generate preliminary data for subsequent application submissions. The NCI anticipates that preliminary studies from the P20s will enable the development of investigator-initiated, multidisciplinary projects (e.g., P01s and/or multidisciplinary R01s). This RFA will support initial studies to establish sufficiently powered or well-curated specimens, feasibility or pilot studies to test exploratory or novel hypotheses, and planning studies to build collaborative teams.

**Subcommittee Review.** Dr. Brawley expressed the Subcommittee's enthusiasm and strong support for the concept. The Subcommittee appreciated the NCI staff responses to its requests to consider that health disparities are rooted in access-to-care factors, not underlying biology, and to address access to care, racism, socioeconomic, and geographic origin in the RFA. The Subcommittee recommended that the NCI clarify whether the underlying premise is to address the efficacy of immunotherapies or the implementation of those therapies. It further suggested refining the scope of the research as results are identified in the pilot projects and considering focusing attention on particular populations and, to a lesser degree, addressing health disparities research broadly.



The first-year cost for the one-time issuance is estimated at \$1 M for two to three P20 awards, with a total cost of \$2 M for 2 years.

## Questions and Answers

NCAB Chair Dr. Carpten suggested specifying in the RFA the types of proposals that are being solicited and providing guidance to the potential applicants. He further commented on using exploratory approaches to begin to address some of the multifactorial issues that are foundational to disparities, including socioeconomic factors; social factors; incidence, risk, and outcome factors; and biological factors. Dr. Doubeni remarked, in this context, on biological differences that are driven by environmental exposures and adverse circumstances.

Dr. Hayes-Jordan highlighted the differences in responses to treatment of the same diagnosis and/or disease beyond cancer, particularly in Black/African American and Hispanic populations. She anticipates that this concept will provide some insight into this clinical problem, which appears to be biology-related. Dr. Earp noted that the microbiome determines a person's response and suggested more research in this area.

**Motion.** A motion to approve the DCB's/OD's new RFA entitled "Integrating Health Disparities into Immuno-Oncology Research (HDIO)" was approved unanimously

## Division of Cancer Treatment and Diagnosis

### **A Data Resource for Analyzing and Supporting Blood and Marrow Transplants and Cellular Immunotherapy Research Center for International Blood and Marrow Transplant Research (CIBMTR) (Re-Issue RFA/Coop. Agr./Limited Competition)—Dr. Lori A. Henderson**

Dr. Lori A. Henderson, Program Director, DCTD, NCI, presented a re-issue RFA concept to continue the Center for International Blood and Marrow Transplant Research (CIBMTR), a data resource for analyzing and supporting blood and marrow transplants and cellular immunotherapy research. The CIBMTR—funded by NCI for more than 30 years and also supported by NHLBI and National Institute of Allergy and Infectious Diseases—has become a world-leading resource. The CIBMTR captures information on hematopoietic stem cell transplant (HCT) and adoptive cell therapies (ACT) for the United States and is essential to researchers, clinicians, and pharmaceutical companies. As an integrated network consisting of transplant centers, a biospecimen biorepository, scientific and statistical expertise, and a clinical database, the CIBMTR is needed to support FDA CAR T-cell product safety and efficacy data and CMS coverage with evidence development trials. The Network also conducts studies to inform clinical trials and practice associated with the treatment of malignant and nonmalignant blood disorders.

Dr. Henderson highlighted some of the CIBMTR's accomplishments. From 2018 to 2020, the Network enrolled 72,000 new cell therapy patients and 5,000 recipients of ACT for transplants or as a primary therapy. In March 2020, the CIBMTR adapted data collection processes to capture detailed information on the diagnosis, treatments, and outcomes of SARS-CoV-2 infections; these data have been reported in five papers published in leading peer-reviewed journals. The Network's Data Transformation Team developed and piloted a technology platform and seven data-sharing apps to expedite data collection. Collectively, CIBMTR investigators published 267 data analysis and research manuscripts. Another hallmark achievement during this time period was the establishment of public-private partnerships to collect CAR T-cell therapy data used to treat hematologic malignancies. The Network partners with the FDA on the required post-marketing safety reporting: five post-marketing studies are in progress. The CIBMTR partners with NCI-funded collaborators on linking clinical outcome data with proteomics and genomics research. Those contributing data include the NCI AIDS Malignancy Consortium (AMC), NHLBI/NCI Blood and Marrow Clinical Trials Network (BMT CTN), and NCI National Clinical Trials Network (NCTN).

The CIBMTR also is a model program for linking data sets to inform clinical practice. Dr. Henderson highlighted two examples. In the first study, real-world data were collected from two Novartis post-market studies for Kymriah<sup>®</sup>, which confirmed the safety and efficacy findings of the ELIANA trial for pediatric treatment of lymphoblastic leukemia, as well as the JULIET trial for non-Hodgkin's lymphoma. In a second study, a large multi-omics project designed to identify genetic and epigenetic and proteomic signatures predicted survival outcomes for myelodysplastic syndrome patients receiving allogeneic transplant.

This RFA re-issuance will enable the CIBMTR to expand HCT and ACT data collection; focus on special initiatives, including HHS evidence-gathering programs; adapt the database for the collection of ACT for solid tumors, as well as new ACT products; and support trial designs and data analyses for observational and interventional studies

**Subcommittee Review.** Dr. Becich expressed the Subcommittee's strong support for the re-issue concept. The Subcommittee congratulated the NCI on having an exceptional program filling a unique niche and a model with demonstrated productivity and success, a trend that is expected to continue.

The first-year cost for the one-time issuance is estimated at \$6.71 M with a total cost of \$33.55 M for 5 years. NCI's contribution is \$4.79 M, NHLBI's \$1.67 M, and NIAID's \$0.25 M per year.

**Motion.** A motion to concur on re-issuance of the DCTD's RFA/Coop. Agr./Limited Competition entitled "A Data Resource for Analyzing and Supporting Blood and Marrow Transplants (CIBMTR)" was approved unanimously.

#### **Division of Cancer Treatment and Diagnosis/Office of the Director**

##### **Patient-Derived Xenograft (PDX) Development and Trial Centers (PDTCs) Network (U54) and PDX Data Commons and Coordinating Center (PDCCC) for the PDXNet (Re-Issue RFA)— Dr. Jeffrey A. Moscow**

Dr. Jeffrey A. Moscow, Chief, Investigational Drug Branch, Cancer Therapy Evaluation Program (CTEP), DCTD, NCI, presented a re-issue RFA concept to continue the PDX Development Network (PDXNet), which is composed of the PDX Development and Trial Centers (PDTCs) and PDX Data Commons and Coordinating Center (PDCCC). The PDXNet was established in 2017, with the goals to test original therapeutic strategies in large-scale PDX collections that could provide preclinical *in vivo* evidence to support novel, early-phase clinical trials; address critical scientific issues related to the use of PDXs as predictive models of clinical benefit through the collaborative network structure of PDXNet; and contribute new PDX models to the NCI Patient-Derived Models Repository (PDMR) for distribution to the wider research community. Two new PDTCs sponsored by the CRCHD joined the Network, and goals were added to increase the diverse representation and study of racial and ethnic minority populations in PDXNet and representation in the PDMR and to advance cancer health disparity research.

Dr. Moscow highlighted accomplishments of the first grant cycle. PDXNet established collaboration with CRCHD to incorporate two M-PDTCs focused on disparity research and developed a culture of collaboration among all grantees, with multiple collaborative research projects. PDXNet investigators contributed 690 unique PDX models to the PDMR and generated 88 publications from original research projects. The Network developed preclinical evidence for 10 CTEP Letters of Intent; launched a website ([pdxnetwork.org](http://pdxnetwork.org)) for internal collaboration and public access; and developed and validated 15 workflows that are publicly shared via the PDXNet portal in support of the collaborative projects.

A program evaluation by an external review committee recognized the progress made by the Network during the funding period even during the COVID-19 pandemic, describing it as impressive. All

reviewers enthusiastically supported renewal of PDXNet, and their summary report noted that important advances in method harmonization, genomic characterization, and developing predictable and well-defined methods had been made. The evaluation concluded that the initiative deserves continued support, having the potential to provide an essential resource for preclinical and clinical cancer research.

This re-issue RFA will support several deliverables. The Network will seek the development and application of drug response evaluation standards across the PDXNet and will advocate adoption of such standards across the wider research community. In this second cycle, efforts will focus on providing robust preclinical *in vivo* data on targeted agent combinations to prioritize at least 20 clinical trials in the NCI clinical trials networks. PDXNet investigators will facilitate more strategic donations of models to the PDMR and will identify and fill significant gaps in the repository collection. The Network will create methods and workflows to integrate complex 'omic and imaging data from multiple sites into a searchable PDX database for model selection and make these tools available. Last, the Network expects to create productive collaborations between PDXNet scientists and early-phase clinical trialists.

**Subcommittee Review.** Dr. David A. Tuveson, Roy J. Zuckerman Professor, Director of the Cancer Center, Cold Spring Harbor Laboratory, expressed the Subcommittee's support for the concept. The Subcommittee commended the NCI for the success of the program, especially the ability to contribute 690 unique PDX models to the PDMR during COVID-19. Dr. Tuveson pointed out that PDXNet is addressing standardization of PDX as a model and noted the value of incorporating models developed into the trial designs. The Subcommittee appreciated the NCI staff responses to its comments and their incorporating its suggestions to improve the program.

The first-year cost for the one-time issuance is estimated at \$8 M for five U54 awards (PDTCs) and one U24 award (PDCCC), with a total cost of \$40 M for 5 years.

### Questions and Answers

Dr. Wicha suggested that the NCI invest in other model systems (e.g., organoids) as comparators for the models developed in the PDTCs.

**Motion.** A motion to concur on re-issuance of the DCTD's/OD's RFA entitled "PDTC Network (U54) and PDX Data Commons and Coordinating Center (PDCCC) for PDXNet" was approved unanimously.

### Division of Cancer Treatment and Diagnosis

#### Systematic Testing of Radionuclides in Preclinical Experiments (STRIPE) (New PAR)— Dr. Michael G. Espey

Dr. Michael G. Espey, Chief, Radiotherapy Development Branch (RDB), Radiation Research Program, DCTD, NCI, presented a new PAR concept to establish the STRIPE program. The goal of this concept is to address knowledge gaps in how radiopharmaceutical therapy (RPT) affects the biology of cancer cells and normal cells and the tumor microenvironment. Dr. Espey explained that, unlike external beam radiotherapy, RPT is targeting based on tumor biology and is useful in local and micro-metastatic disease. RPT has desirable modular qualities conducive to a variety of molecular targeting approaches, including nanotechnology and engineered cancer-specific antibodies.

A portfolio analysis of the state of the RPT field revealed that several RPT agents have clinical effects for difficult-to-treat neuroendocrine and metastatic cancers, but the preclinical space is limited. The NCI research portfolio in RPT currently consists of 20 grants focused on therapeutic or imaging-based objectives, with minimal support in understanding the radiobiology of RPT. The NCI is proposing the STRIPE program to address unmet needs in foundational preclinical RPT. The central objective is to catalyze collaborative projects that strengthen the preclinical foundation of the RPT field. The program

will facilitate integration of RPT into preclinical-oriented tumor biology experiments, with the potential to identify new targeting strategies and conduct a more systematic examination of drug RPT combinations.

**Subcommittee Review.** Dr. Karen E. Knudsen, Chief Executive Officer, American Cancer Society, Inc., American Cancer Society Cancer Action Network, expressed the Subcommittee’s enthusiasm and support for the concept, which addresses an important area to increase the pace of discovery. The Subcommittee pointed out that this concept addresses an unmet need and brings needed collaboration between pharmaceutical scientists and cancer biologists.

**Motion.** A motion to approve the DCTD’s new PAR entitled “Systematic Testing of Radionuclides in Preclinical Experiments (STRIPE) was approved with 12 ayes, 0 nays, and 1 abstention.

### Office of the Director

#### **Informatics Technology for Cancer Research (Re-Issue RFA/Coop. Agr.)—Dr. Juli Klemm**

Dr. Juli Klemm, Program Director, Center for Strategic Scientific Initiatives, NCI, presented a re-issue RFA concept for the Informatics Technology for Cancer Research (ITCR) program. The ITCR, which launched in 2013, is an NCI-wide program that supports investigator-initiated informatics technology development, driven by critical needs in cancer research. Funded projects support a range of cancer research activities, and tools developed through ITCR are open source. Programmatic activities promote interoperability and dissemination of the supported tools.

The current ITCR program structure supports activities across the informatics development life cycle, from algorithm development to sustainment, all through a series of companion funding opportunities. Four RFAs support informatics technology development. An R21 supports the development of innovative methods and algorithms. The U01 supports early-stage tool development. The advanced development U24 supports the enhancement and dissemination of emerging informatics tools. The sustainment U24 supports highly accessed mature informatics resources. The U01 and U24 awardees are required to set aside 10 percent of their annual budget for collaborative activities that are proposed post-award. In addition, a new education resource was added to the program at its last renewal for conducting activities that engage the research and informatics community to use and extend the ITCR technologies. The program has offered a series of competitive revisions to support the incorporation of ITCR-funded technology into NCI-funded R01, U01, and U24 projects.

Since its inception, the ITCR program has made several accomplishments. For example, tools supported through the program are among the most widely used informatics resources in cancer research and are supporting important advances across the cancer research continuum. The program is fostering a community of practice in cancer informatics, through programmatic emphasis on collaboration and interoperability that is supported through the set-aside funds. The set-aside funds have supported more than 50 alliances that have led to the emergence of the ecosystem of cancer informatics resources. ITCR tools have high adoption and citation rates due to an emphasis on outreach and training. To date, the ITCR has made 130 awards, and the portfolio of tools supports a wide range of data types. The most prominent are technologies to support radiology imaging, medical informatics, genomics, and histology. The program maintains an online catalog of the ITCR-supported tools.

Activities to promote dissemination of ITCR tools include focused journal issues, presence at scientific conferences, webinar series, NCI scientific program meetings, social media, and the Training and Outreach Working Group. In response to recommendations from the 2018 program evaluation, the ITCR added an Informatics Technology for Cancer Research Education Resource (UE5). Johns Hopkins University was awarded the first ITCR UE5 in September 2020 and initiated the ITCR Training Network (ITN), which recently launched two online courses on “Leadership for Cancer Informatics” and “Dissemination and Usability.”

A program evaluation by an external review committee in 2021 identified several strengths, with the overall recommendation to continue the program as structured. Other recommendations were to continue to promote collaborations among tool developers, emphasize emerging technologies to keep pace with advances in cancer research, and maximize the value of the technologies.

This re-issue RFA will support the ITCR to continue to employ a multimechanism approach—using the R21, U01, and U24 mechanisms—to fund informatics technology development. The program will continue to make the funding opportunity announcements, clinical trials optional, to support technology validation studies that meet the NIH definition of a clinical trial. The ITCR program team will optimize processes to prioritize meritorious R21 and U01 applications for inclusion in funding plans and promote academic and industry partnerships. The NCI Small Business Innovation Research program will be engaged to identify opportunities for collaboration with industrial partners through directed outreach and focused contract topics.

**Subcommittee Review.** Dr. Sylvia Plevritis, Chair and Professor of Biomedical Data Science, Professor of Radiology, Director, Biomedical Informatics Graduate Program, Stanford University School of Medicine, expressed the Subcommittee’s strong support for the concept. The Subcommittee suggested that the NCI explore ways of integrating the ITCR with other key NCI programs.

The first-year cost for the one-time re-issuance is estimated at \$8 M for five R21 awards, five U01 awards, four U24 advanced development awards, and one U24 sustainment award, with a total cost of \$40 M for 5 years.

### Questions and Answers

NCAB Chair Dr. Carpten suggested enhancing data science and bioinformatics training in underrepresented minority institutions.

**Motion.** A motion to concur on re-issuance of the OD’s RFA/Coop. Agr. entitled “Informatics Technology for Cancer Research” was approved unanimously.

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

**NCAB *ad hoc* Experimental Therapeutics Subcommittee.** Dr. Ley, Chair of the NCAB *ad hoc* Experimental Therapeutics Subcommittee, presented the report of the 7 December 2021 meeting. In an overview of the Subcommittee activities, he noted that the NCI Director, Dr. Sharpless, attended the meeting and charged the Subcommittee to advise the NCI leadership about emerging experimental topics that are relevant for NCI investment in the future. Dr. Ley noted that following the charge, the Subcommittee met, considered a wide variety of topics, and selected two to address: cellular therapy and rational drug discovery. Members were informed that NCI staff, particularly Dr. Rose Aurigemma, the Executive Secretary of the Subcommittee, organized and convened two NCI workshops on cellular therapy, which resulted in a report consisting of seven recommendations that were presented to and subsequently approved by the NCAB.

Dr. Ley called attention to an October 2021 meeting on the rational drug discovery in which four topics were discussed: virtual biology; cryo-EM; machine learning/artificial intelligence; and target interrogation. Several themes emerged from the workshop, of which Dr. Aurigemma presented a draft at the 7 December 2021 meeting of this Subcommittee. In her report, Dr. Aurigemma detailed the overarching themes about areas that are very problematic in this field. Dr. Ley summarized that the Subcommittee was informed of data sharing and homogenization as an obstacle to developing databases.

Reproducibility of studies should be addressed. Unification of investigators in academia and in the pharmaceutical industry remains an issue as well as ways to address the “idea” to a product. The Subcommittee was updated on the recommendations from the workshop relevant to the NCI, including developing mechanisms for evaluating non-druggable targets and increasing the accessibility of the libraries that are in the NExT Program. Dr. Ley expressed appreciation to Dr. Aurigemma and her team for the report.

### Questions and Answers

Dr. Sharpless suggested a presentation on the NCAB *ad hoc* Experimental Therapeutics Subcommittee priority topics at a future Board meeting.

Dr. Doubeni asked whether other NIH Institutes were doing drug development and could provide a roadmap. Dr. Sharpless noted the collaborations with the National Center for Advancing Translational Sciences on high-throughput screening and robotic approaches to scientific screening and interest from NIAID on novel data approaches to drug discovery and machine learning in drug discovery. NIH-wide interest in this topic could inform a CF effort.

**Motion.** A motion to accept the report of the 7 December 2021 NCAB *ad hoc* Subcommittee on Experimental Therapeutics meeting was approved unanimously.

**Other Business.** Dr. Plevritis proposed establishing a committee to provide guidance on leveraging bioinformatics infrastructures and implementing an informatics mandate in large NCI programs (e.g., CCSGs) through greater integration with the Informatics Technology for Cancer Research and other major programs.

**Future Agenda Items.** The BSA and NCAB members suggested future presentations on education and training opportunities in the NCI; obesity; the DCCPS director’s vision for the future; capacity building efforts in international activities, including the NIH Fogarty International Center; and crosscutting research between NCI and the National Institute on Aging. Members were asked to forward any additional suggestions for potential future agenda items to the respective Board chairs and Dr. Gray.

**XVI. 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 5<sup>th</sup> Virtual Joint Meeting of the BSA and NCAB was adjourned at 5:29 p.m. on Thursday, 9 December 2021.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Keith T. Flaherty, M.D., Chair, BSA

\_\_\_\_\_  
Date

\_\_\_\_\_  
John D. Carpten, Ph.D., Chair, NCAB

\_\_\_\_\_  
Date

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