

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

**57<sup>th</sup> Meeting**

**BOARD OF SCIENTIFIC ADVISORS**

**Minutes of Meeting**

**March 29, 2016  
Building 31C, Conference Room 10  
Bethesda, Maryland**

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

**BOARD OF SCIENTIFIC ADVISORS**

**MINUTES OF MEETING**

**March 29, 2016**

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 56<sup>th</sup> meeting on Tuesday, 29 March 2016, at 9:00 a.m. in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Chi V. Dang, Director, Abraham Cancer Center, Professor of Medicine, Perelman School of Medicine, University of Pennsylvania, presided as Chair. The meeting was open to the public from 9:00 a.m. until 3:38 p.m. on 29 March for the NCI Acting Director's report; a legislative report; an update report on Cancer Centers funding policy metrics; a report from the Tobacco Control Research Priorities Working Group; and consideration of request for applications (RFA) and request for proposal (RFP) new and reissue concepts presented by NCI Program staff.

**BSA Board Members Present:**

Dr. Chi V. Dang (Chair)  
Dr. Francis Ali-Osman  
Dr. Kenneth C. Anderson  
Dr. Dafna Bar-Sagi  
Dr. Ethan M. Basch  
Dr. Sangeeta N. Bhatia  
Dr. Andrea Califano  
Dr. Arul M. Chinnaiyan  
Dr. Graham A. Colditz  
Dr. Daniel C. DiMaio  
Dr. Karen M. Emmons  
Dr. Carol E. Ferrans  
Dr. Stanton L. Gerson  
Dr. Chanita Hughes-Halbert  
Dr. James V. Lacey  
Dr. Theodore S. Lawrence  
Dr. Maria Elena Martinez

Ms. Diane Zipursky Quale  
Dr. Martine F. Roussel (Sherr)  
Dr. Victoria L. Seewaldt  
Dr. Kevin M. Shannon  
Dr. Mary L. Smith  
Dr. Lincoln D. Stein  
Dr. Eileen P. White

**Board Members Absent:**

Dr. Joseph M. DeSimone  
Dr. Brian J. Druker  
Dr. Joe W. Gray  
Dr. Luis F. Parada  
Dr. Gregory L. Verdine  
Dr. Cheryl L. Walker  
Dr. Kevin P. White

**Others present:** Members of NCI's Scientific Program Leaders (SPL), NCI staff, members of the extramural community, and press representatives.

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### I. CALL TO ORDER AND OPENING REMARKS—DR. CHI V. DANG

Dr. Chi V. Dang called to order the 57<sup>th</sup> regular meeting of the BSA and welcomed current members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Dang reminded Board members of the conflict-of-interest guidelines and confidentiality requirements. Members of the public were invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

### II. NCI ACTING DIRECTOR’S REPORT—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Acting Director, welcomed members of the BSA, provided an update on the NCI’s budget, and described NCI’s activities related to the Vice President’s Cancer Initiative (also referred to as the Cancer Moonshot). Dr. Lowy recognized the promotions of Drs. Dinah S. Singer, Director, Division of Cancer Biology (DCB), and Warren Kibbe, Director, Center for Biomedical Informatics and Information Technology (CBIIT), to positions of NCI Acting Deputy Directors to assist with the Cancer Moonshot.

**Outlook for Cancer Research Funding.** Dr. Lowy described the positive outlook for cancer research funding, referencing strong Congressional bipartisan support for the NCI and NIH in terms of cancer research opportunities, key role of advocacy, and faster progress for patients. He also noted the potential for continuing increases in Federal cancer research funding and affirmed NCI’s continued commitment toward coordination with private funding efforts.

Members were informed that the fiscal year (FY) 2016 appropriations for the NCI include an additional \$265 million (M), which reflects a 5 percent increase over the FY 2015 level and includes \$70 M for the President’s Precision Medicine Initiative in Oncology (PMI-O). Members were told that funding for research project grants (RPGs) in FY 2016 provides an additional \$50 M to noncompeting awards to ensure continued support at 100 percent commitment levels, and an additional \$53 M to the \$447 M that became available from awards that were ending to provide \$500 million for new and competing awards.

Dr. Lowy reflected on the encouraging trend in the budget for FY 2016 and 2017, noting that the NCI has maintained its purchasing power from 2012 through 2016, and a substantial increase of \$680 million is proposed in the President's budget for FY2017.

**The Vice President's Cancer Initiative (Cancer Moonshot).** Dr. Lowy stated that the initiative aims to accelerate progress in cancer, including prevention and screening and cutting-edge basic research to facilitate a wider uptake of standard of care. The Initiative will encourage greater cooperation and breaking down of silos within and between academia, government, and the private sector. It also will focus on the importance of data sharing, including the Genomic Data Commons, annotated patient-level clinical data, and the -omics. He noted that Vice President Joseph Biden expressed his long-term commitment to the initiative and enthusiasm for the opportunity to fundamentally change the trajectory of cancer in terms of prevention, early detection, and treatment.

Members were told that prevention, screening and implementation activities proposed include development of preventive interventions (such as vaccines against infectious and noninfectious targets), development of screening tests with bodily fluid samples, and to increase uptake of the standard of care. Clinical and preclinical activities addressing cancer treatment include increasing immunotherapy trials and combination therapy trials; increasing patient participation in clinical trials; developing new treatments for pediatric cancer; developing a virtual drug formulary at the NCI incorporating agents from many companies to facilitate the study of combination therapy; and expanding -omic analysis of tumor and stromal cells for patients with clinical annotation. Other proposed research aims are to develop drugs for pediatric cancer, increase preclinical studies of therapeutic cancer vaccines and cancer immunotherapy, increase basic research, especially in immunology, and develop an exceptional opportunities fund.

Dr. Singer provided an overview of the initiative, including its formation, constituency, structure, and proposed timeline. She noted that the Vice President's office oversees the Cancer Moonshot and receives advice from the Cancer Moonshot Federal Task Force, which is composed of representatives from 13 agencies including the NIH, NCI, U.S. Food and Drug Administration (FDA), Department of Defense (DOD), Veterans Administration (VA), Department of Energy (DOE), National Science Foundation (NSF). The goals of the Cancer Moonshot are to accelerate understanding of cancer; support greater access to new research, data, and computational capabilities; improve patient access and care; address unnecessary regulatory barriers; and identify opportunities to develop public-private partnerships.

A Blue Ribbon Panel will be established and will report to the National Cancer Advisory Board (NCAB), with the charge to provide expert advice on the vision, proposed scientific goals, and implementation of the Cancer Moonshot. Working groups will be formed around specific topic areas, and public participation in the Initiative will be take place through an online public idea repository, email, workshops, and professional meetings. In late summer, the Panel will submit its report on high-priority ideas to the NCAB, which will provide recommendations to the NCI. Dr. Singer reviewed the proposed timeline for funding opportunity announcements (FOAs), with FOAs being prepared in August–October 2016, to meet the goal of reviewing and funding awards in FY2017.

Dr. James H. Doroshow, Deputy Director, described NCI's activities to develop a virtual drug formulary through which the NCI would distribute drugs for studies, manage overall quality control, and facilitate intellectual property (IP) rights arrangements with a large number of companies. The NCI hopes to meet many interested companies at the American Society of Clinical Oncology (ASCO) annual meeting, and Vice President Biden has indicated his willingness to interact with pharmaceutical companies to facilitate access to drug compounds.

**Precision Medicine Initiative in Oncology (PMI-O).** Dr. Doroshow informed members about activities related to the PMI-O, including a recent workshop in immunotherapy at which significant interest was

expressed to further develop T-cell adoptive immunotherapy, as well as platforms for translational support to fully understand the pharmacodynamic and molecular effects of immunotherapies in the context of tumors and stromal cells. Other related activities include a workshop on patient-derived xenografts (PDX) and the forthcoming PDX repository, with plans to distribute the first cell lines and models around July 2016.

**In the discussion, the following points were made:**

- A key component of the virtual formulary's success will be agreement of all parties on adopting the standard IP framework used for all of NCI-supported clinical trials.
- The intent of the formulary is to accelerate access to compounds for many trials, and access is not limited to only NCI-supported trials. The greatest interest in the virtual drug formulary likely will be for investigator-derived, investigator basic science-supported combinations in early phase trials. The NCI-Molecular Analysis for Therapy Choice (MATCH) trial's current work in conducting parallel trials that involve several agents against a particular target from different companies may provide a model for the virtual formulary.
- The predictive value of preclinical models and an integrated pipeline for preclinical testing are topics that the Blue Ribbon Panel Working Groups likely will discuss. Plans include looking at canine models and development of additional cell lines. Older potentially virally induced mutagenesis models and chemical carcinogenesis models could be resurrected now that the technologies are available to characterize specimens deeply at a molecular level.
- Members suggested that the Cancer Moonshot Task Force work to accelerate the elimination of silos to ensure that information learned at one institution is widely disseminated and shared and that collaboration among investigators from distinct institutions is encouraged.
- The Blue Ribbon Panel has the role of providing recommendations about research priorities, and the NCI will develop benchmarks when planning implementation of the priority areas. Members encouraged the Blue Ribbon Panel to include adequate specificity in its recommendations to the NCAB to ensure that the public understands that goals are achievable. The BSA will have the opportunity to engage in the Initiative through its Joint Board meetings with the NCAB.
- The NCI could play a stronger role in promoting the standard of care by encouraging the Cancer Centers to implement strategies related to prevention and screening, such as reducing tobacco use as a cancer control strategy.
- Members suggested that the NCI take advantage of partnerships and other opportunities to expedite the use of novel, transformative, and complementary technologies, such as liquid biopsies, cell-free nucleic acids, and nanosensors. Dr. Lowy indicated that technologies will be considered by the Blue Ribbon Panel Working Groups and could be supported through the Exceptional Opportunities Initiative.
- Members recommended that the NCI capitalize on existing experience in the area of implementation science to expand capacity in the field and also encouraged sensitivity to health disparities.
- Molecular abnormalities and the reasons some patients respond well to treatment are key areas in precision oncology that need to be understood before dissemination of standard of care can be addressed.

### **III. NCI/CONGRESSIONAL RELATIONS—MS. M.K. HOLOHAN**

Ms. M.K. Holohan, Director, Office of Congressional Relations (OCR), provided an update on the status of appropriations and hearings, and highlighted key events relevant to the VPCI's Cancer Moonshot Initiative. Ms. Holohan reminded members that the NCI receives its funding as part of the overall Federal budget process. The budget approved in November 2015 raised budget caps and allowed more funding for FY 2016 and 2017. Strong bipartisan support for the NIH resulted in a \$2 billion (B) increase in funding for the NIH in FY 2016, including a \$265 M increase for the NCI. Current authorizing bills of interest include the 21st Century Cures, which passed the House with mandatory funding for the NIH, and the Innovation Act currently under consideration in the Senate.

The FY 2017 President's Budget requests \$82.8 B for the Department of Health and Human Services' discretionary programs, reflecting a \$1 B cut to the NIH for discretionary funding. Increases to mandatory funding, however, would add \$1.8 B for the NIH, including \$680 M for the Vice President's Cancer Initiative. Ms. Holohan noted that the House has been debating for weeks about a budget resolution concerning discretionary funding and described discretionary caps, an emergency funding category that provides relief from the caps, and other current budget control tools in place under which Congressional committees operate. The authorizers are looking for a way to supplement appropriated funds to move forward on the Cancer Moonshot in FY2017.

Ms. Holohan described a visit by House Appropriators to the NIH on February 29, 2016, as well as support expressed by the House Appropriations Committee at an NIH Budget Hearing on March 16, 2016, at which Dr. Lowy provided testimony. Members were informed that Vice President Biden named Greg Simon as the Executive Director of the Cancer Moonshot Task Force on March 18, and a Senate Appropriations Hearing on the NIH budget is scheduled for April 7, 2016.

### **IV. UPDATE: CANCER CENTERS FUNDING POLICY METRICS—DR. HENRY P. CIOLINO**

Dr. Henry P. Ciolino, Acting Director, Office of Cancer Centers, provided an update on the funding policy metrics for NCI-designated Cancer Centers. Dr. Ciolino stated that the NCI leadership worked closely with the BSA Cancer Centers Working Group and the NCAB to rebalance funding phases to minimize inequalities among NCI-designated Cancer Centers. The first phase will establish base awards by type—specifically basic, clinical, or comprehensive Center—and will result in all Centers being brought up to the new base in FY 2016, as recommended by the NCAB. The second phase will be implemented during FY 2018–2022 and will allocate new NCI Cancer Center Support Grant (CCSG) funds using NCAB-recommended metrics on the size of the research base of a Center and the merit score achieved during the review of its next competitive application. Commencing in FY 2023, the third phase will either continue the effort with more new money or adopt a zero-based formula using the metrics recommended by the NCAB.

Dr. Ciolino stated that the new base awards will rebalance base funding for approximately 50 percent of the Cancer Centers, with notable increases for 21 Centers. A new benchmark base ratio of 15 percent will be used to determine a Comprehensive Cancer Center's maximum award and the percent will gradually decrease for larger cancer centers with greater than \$20 M in cancer research funding. The CCSG merit score will be used to determine the ultimate direct cost award. Members were reminded that the Board approved the BSA Cancer Centers Working Group's report unanimously in December 2015, with stipulations that NCI leadership consider the inclusion of non-NCI funding sources, criteria to evaluate the cancer relevance of those sources, and the potential advantages or disadvantages bestowed on individual Centers through such inclusion. Dr. Ciolino described the core principles, which include that the calculation of budget eligibility should neither affect how Centers write their application nor depend

on reviewers, estimates of cancer relevance must be objective and apply to all grants, and the process must be simple and transparent. He noted that increasing the funding base, however, requires a decrease in the benchmark ratio to remain within budget. The NIH RePORTER's Research, Condition, and Disease Categorization (RCDC) feature will be used, as it allows an independent assessment of a Center's portfolio, determines cancer relevance objectively by measuring all NIH grants by the same standards, provides a simple and transparent evaluation, and can accommodate Centers with members who receive significant cancer-focused grants from other NIH Institutes. Dr. Ciolino compared the effect of the new funding policy on the funding base of four Centers based on FY 2014 data, illustrating the shifts in budget eligibility for the Centers when all their NIH funding is considered.

Members were told that the Cancer Centers Working Group recommended unanimously to exclude all non-NIH funding because there is no way to independently verify funding, inclusion would complicate the budget calculation, and funding from some organizations is not available to all Centers. Dr. Ciolino noted that non-NIH sources represent 17 percent of all funding reported by the Centers. He cautioned that the proposed funding policy has not been implemented previously in the Program and unexpected outcomes in merit review were likely to require some policy adjustment.

**In the discussion, the following points were made:**

- The BSA Cancer Centers Working Group worked closely with NCI Centers Program staff to identify the simplest and most equitable way to calculate the distribution of funding among NCI-designated Centers.
- In response to concerns raised about the exclusion of non-NIH funding in areas where funding has systematically shifted to other agencies and organizations, such as cancer control and population sciences, Dr. Dang clarified that all relevant funding can be included for the evaluation of merit, but only NCI and NIH funding would be considered in the funding calculation.
- Staff confirmed that the RCDC data on current cancer research funding is readily available to view online.

**V. TOBACCO CONTROL RESEARCH PRIORITIES WORKING GROUP REPORT—  
DRS. ROBERT T. CROYLE, ROBIN MERMELSTEIN, AND MICHAEL C. FIORE**

Dr. Robert T. Croyle, Director, Division of Cancer Control and Population Sciences (DCCPS), provided a brief overview and context for the BSA Tobacco Control Working Group, which was charged with conducting a focused review of the tobacco control landscape. He introduced the Working Group Co-Chairs, who reported the Working Group's findings and recommendations: Drs. Robin Mermelstein, Director, Institute for Health Research and Policy, University of Illinois; and Michael C. Fiore, Director, Center for Tobacco Research and Intervention, University of Wisconsin School of Medicine and Public Health.

Dr. Fiore discussed the context of the tobacco control report and provided a review of the epidemiologic imperatives regarding tobacco use in America today. The 2014 Surgeon General's report, *The Health Consequences of Smoking—50 Years of Progress*, outlined a national strategy to end tobacco use in America. He noted two misconceptions that have impeded the goal of the national strategy: (1) that the tobacco problem in America had been solved and (2) that all of the key tobacco control research questions had been answered. Although significant progress has been achieved in reducing the rates of tobacco use from 43 percent in the 1960s to 17 percent in 2014, the challenge is to define strategies that will accelerate progress to eliminate tobacco use in America over the next 2 decades.

Dr. Fiore stated that approximately 45 million adults in the United States smoke cigarettes, resulting in more than 500 million deaths from diseases directly related to smoking. On average, 1 out of 5 deaths can be attributed to smoking. One-third of all cancer deaths are attributable to smoking, and smoking is a direct cause of at least 13 types of cancer, including 80 to 90 percent of all lung cancers. In addition to the mortality and morbidity, tobacco use also is responsible for nearly \$200 B in added medical costs.

The toll of tobacco use is not equal across the demographics of the American society, and is more harmful to disadvantaged populations. Smoking rates based on economic status show that the rates were higher in adults below the poverty level than for those above the poverty level. In addition, an inverse relationship has been reported between education and the smoking rate, in which smoking increases with decreasing education status. Co-behaviors of alcohol abuse and tobacco use also are correlative, and data suggest that alcohol abusers are more likely to succumb to tobacco-related illnesses. In addition, an estimated 14.2 million smokers have serious psychological distress, and smoking rates are higher in mentally ill populations. Increased attention must be focused on these vulnerable populations to eliminate tobacco use in the United States.

Dr. Fiore briefly described the Tobacco Control Working Group's process for preparing the research priorities report, including two in-person meetings and communications via digital media. The Working Group engaged other public and nonprofit research funders and tobacco control stakeholders, including the National Institute on Drug Abuse (NIDA), FDA, Centers for Disease Control and Prevention's (CDC) Office on Smoking and Health, Truth Initiative, and Campaign for Tobacco Free Kids, to provide perspective on the tobacco control research landscape.

Dr. Mermelstein provided an overview of the Tobacco Control Working Group's recommendations for research priorities for the next decade and stated that they were broad in scope, overlapping, and of equal importance. Recommendations covered seven high priority research areas that would have the greatest potential of eliminating the harmful effects of tobacco use in the United States, including smoking-related cancers: (1) Optimize intervention effectiveness by increasing the reach, demand, quality, dissemination, implementation, and sustainability of tobacco use treatment; (2) Reduce adolescent and young adult tobacco use by identifying research that informs and reflects societal changes and changes in the tobacco product landscape; (3) Address disparities in tobacco use to directly target and improve treatment effectiveness and increase understanding of population specific contextual approaches and environmental factors; (4) Understand the complexity of current tobacco products, patterns of use, and associated health-related outcomes by researching their short- and long-term effects on cancer and other health risks; (5) Develop novel behavioral interventions for tobacco use to accelerate treatment effectiveness by using treatment algorithms and adaptive designs for personalizing treatments; (6) Use a chronic disease approach to address smoking behavior across all developmental phases by researching all phases of cessation from motivation through relapse and post-relapse recovery; and (7) Identify innovative policy approaches that further reduce tobacco use and effective strategies to provide a more complete dissemination of the innovative approaches.

In addition to the seven priority areas, the Tobacco Control Working Group identified several cross-cutting research infrastructure steps that would help accelerate research progress in each of the priority areas. These included developing a clinical trials network to facilitate innovative and collaborative tobacco research needs, enhancing recruitment of special populations, establishing rapid funding mechanisms to support important emerging research initiatives in a timely manner, and encouraging more pragmatic and innovative methods in study designs. A full summary of the Working Group's recommendations can be found in its report, *Tobacco Control Research Priorities for the Next Decade: Working Group Recommendations for 2016–2025*.

**In the discussion, the following points were made:**

- The Tobacco Control Working Group’s scope focused on combustible tobacco cigarettes because alternative nicotine delivery systems, such as e-cigarettes, reside within the FDA’s purview of regulatory science. The Working Group highlighted the use of e-cigarettes as a potential pathway to combustibles as a research priority.
- Members suggested that the factors that contributed to the decline of prevalence in the past be identified because those factors may accelerate further declines.
- The relevance of different cancer etiology factors should be considered for disparate populations.
- Highly targeted interventions should be developed to address the smoking population afflicted with mental disease, as well as strategies to identify adolescents in crisis to discourage addictive behaviors.
- NCI’s portfolio includes studies on harnessing Facebook, social media, and text applications for reaching young adults, as well as an outreach to tobacco users called Smokefree.gov.
- The effects of co-use of combustible tobacco and marijuana is an important policy question as states legalize or decriminalize marijuana, including the development of dependence on tobacco through marijuana use.
- Members suggested that consideration be given to leveraging studies using state quit lines since it provides the opportunity for a population wide approach.
- The research programs, interventions, and lessons learned in helping smokers also could be applicable to obesity, particularly as both affect underserved and disadvantaged populations.
- Members encouraged researchers to think about digital health and the premise of reaching and connecting those dealing with health conditions (smoking, obesity) through better eTools.

## **VI. RFA/COOPERATIVE AGREEMENT CONCEPTS—NCI PROGRAM STAFF**

### **Office of the Director (OD)**

#### **U.S.–Russia Bilateral Collaborative Research Partnerships on Cancer (New RFA)**

Dr. Paul Pearlman, Center for Global Health (CGH), presented a new concept for a bilateral collaborative research partnership on cancer with Russia. Dr. Pearlman noted that the NCI and NIH have participated in jointly funded programs with several countries, including China, Brazil, South Africa, and Turkey, and that the concept has the support of the U.S. Department of State and Mr. John F. Tefft, U.S. Ambassador to Russia. Two previous NIH FOAs led by the Office of AIDS Research (OAR) focused on collaboration with Russia on HIV- and AIDS-associated work. In addition, Dr. Lowy signed a Memorandum of Understanding (MOU) recently with the Russian Foundation for Basic Research (RFBR) Foundation that this concept seeks to put into practice. In October 2015, an NCI delegation visited the RFBR in Moscow and negotiated an initial list of collaboration topics that has been expanded to include immunotherapy and the tumor microenvironment; targeted delivery of anticancer drugs; brain tumors; nanoparticles; epigenetics, proteomics, and metabolomics; biomarkers; physical sciences and engineering in cancer biology; and radiation epidemiology. The plans for this RFA is to issue ten awards (R21) for a maximum of \$100,000 direct costs per year for three years. Approximately 10 percent of funding requested will be

reserved to support intramural research collaborations, similar to previous bilateral co-funding opportunities. Funded awards will be determined after simultaneous NCI and RFBR review.

**Subcommittee Review.** Dr. Stanton L. Gerson, Shiverick Professor of Hematological Oncology, Director, Case Comprehensive Cancer Center, Director, National Center for Regenerative Medicine, Case Western Reserve University, and Director, Siedman Cancer Center, University Hospitals Case Medical Center, expressed the Subcommittee's support for the concept. Dr. Gerson encouraged NCI staff to promote funding sustainability through more formal partnerships between organizations, collaboration between investigators, and exchange programs for students. The Subcommittee expressed concerns about the broad topic list and the review process.

**In the discussion, the following points were made:**

- NCI Program staff confirmed that the intent is to fund all 10 grants in Year 1, provided that sufficient high-quality applications are submitted. Long-term success would be to establish sustained research that is competitive in the individual investigator (R01) pool.
- Staff clarified that the initial list of topics ensued from the RFBR Foundation's areas of interest. Reviews will be done separately at NCI and RFBR, then they will come together to negotiate on final awards.
- The bilateral approach provides a feasible vehicle to collaborate with a foreign partner on shared priority areas while accommodating the scientific interests, administrative organization, and funding structures of the partnering country.

The first year's cost is estimated at \$1.85 M for 10 R21 awards, with a total cost of \$5.55 M for 3 years.

**Motion.** A motion to concur on the Office of the Director's (OD) RFA entitled "U.S.-Russia Bilateral Collaborative Research Partnerships on Cancer" was approved unanimously.

**Division of Cancer Control and Population Sciences (DCCPS)**

**Research to Optimize Screening Processes in Diverse Populations (PROSPR) (Reissue RFA/Coop. Agr.)**

Dr. Stephen Taplin, DCCPS, presented a reissuance concept on the Research to Optimize Screening Processes in Diverse Populations (PROSPR) Program that aims to change organizational and provider factors to improve screening, address differential screening across race and ethnicity, provide common measures of quality, and develop ways to measure and achieve improved screening in the United States. PROSPR was initiated because mortality reductions were shown to be possible through screening, and the current program has focused on documenting the screening process across breast, cervical, and colorectal cancers, with seven centers funded to conduct projects relevant to understanding and improving the process. The centers have captured large diverse populations—including Caucasian, African American, and Hispanic race and ethnicities—and have shown that screening process variations among populations can have a large impact. The organizational and provider factors that affect the screening process remain to be determined, as do how to measure the quality of the screening process, long-term effects of screening, and interventions that could improve the screening process.

The reissuance places a greater emphasis on disparities; expands data available for screening studies, such as by increasing longitudinal follow up and adding lung cancer screening; and establishes metrics of patient, provider, and system factors that affect the screening process. It also will evaluate the quality of the screening process in terms of effectiveness, safety, patient-centeredness, timeliness, efficiency, and

equity and will intervene at some step in the process after screening occurs. The concept includes four research centers that each will cover one cancer type but together will address at least two systems of care in a collaborative application and provide representation of diverse populations. A Coordinating Center will be responsible for data aggregation, the annual export of the data set, and oversight of quality measurement across cancers.

**Subcommittee Review.** Dr. Chanita Hughes-Halbert, Professor and Endowed Chair, Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Hollings Cancer Center, expressed the Subcommittee's support for the reissuance through an open competition process and its emphasis on geographic and racial/ethnic disparities. Dr. Hughes-Halbert noted that the current PROSPR Program includes productive consortia members who have examined a wide range of issues related to screening, commended the inclusion of organizational and provider factors to be measured as one way to evaluate interventions that address high-quality screening, and suggested that the concept include metrics for patient-level data on social determinants. The Subcommittee encouraged Program staff to consider strategies to ensure better minority representation for a given cancer and more data about the populations, as well as to require that the awardees standardize their measurements across organizations.

**In the discussion, the following points were made:**

- Program staff clarified that the concept uses the Cancer Intervention and Surveillance Modeling Network (CISNET) model to encourage the groups submitting an application to think about a joint set of science from the outset. It also includes a requirement to describe an intervention that would address a potential problem in the screening process.
- Members commented on the limitations of mammography in screening for triple-negative breast cancer in the absence of a mass and encouraged the Program to look at the types of breast cancer that were identified by the screening. Consortia members could form partnerships with additional networks and providers, such as Federally Qualified Community Health Centers and NCI Community Oncology Research Program (NCORP), to gain access to many different populations experiencing disparities.
- Members discussed incentivizing existing PROSPR centers to increase the numbers of underserved populations in screening trials as an alternative to an open competition.
- Members commented that centers should be encouraged to attract more diverse populations from underserved sites across the country through specific criteria in the FOA.

The first year's cost is estimated at \$12 M for four U01 awards and \$1.5 M for one U54 award, with a total cost of \$67.5 M for 5 years.

**Motion.** A motion to concur on the Division of Cancer Control and Population Sciences' (DCCPS) reissue RFA/Coop. Agr. entitled "Research to Optimize Screening Processes in Diverse Populations" was approved unanimously. A motion to amend the PROSPR RFA/Coop. Agr. to require PROSPR applicants to demonstrate the capability to recruit diverse and underserved populations was approved with 23 ayes, 0 nays, and 1 abstention.

## Office of the Director (OD)

### Cancer Target Discovery and Development Network Centers (CTD<sup>2</sup>) (Reissue RFA/Coop. Agr.)

Dr. Daniela S. Gerhard, Center for Cancer Genomics (CCG), presented the reissue concept for the Cancer Target Discovery and Development Network Centers (CTD<sup>2</sup>). The CTD<sup>2</sup> Network developed multidisciplinary teams that use genome-scale experimental approaches to explain cellular functions in genes that cannot be understood through sequencing and to identify cancer drivers, therapeutic targets, predictive biomarkers, and perturbagens (e.g., small molecules, RNAi, etc.) across multiple cancers. Thirteen Centers collaborate, interact, and share data through a public CTD<sup>2</sup> Network, a dashboard and an intra-Network data portal to effectively address the major scientific challenges in cancer research—from large, multidimensional genomic data to target validation, small molecular modulators, and therapies. The Network's website includes analytic tools and publications produced by the Centers. More than 130 publications have resulted, with 20 cited more than 40 times. Examples of the Network's ability to shift paradigms in the translation of patient-derived genetic data to the clinic include a high-throughput method that functionally characterized the most frequent mutation of *PIK3RI* and a new CRISPR/Cas9 genome-editing tool to precisely modify human T cells.

The reissue concept aims to integrate new genomic data into the bioinformatics component, which currently includes The Cancer Genome Atlas (TCGA), Therapeutically Applicable Research to Generate Effective Treatments (TARGET), and the Cancer Genome Characterization Initiative (CGCI). Another goal is to accelerate the translation of patient genomic data into clinical application by integrating computational mining, large-scale genomic data analyses, and N-of-1 applications, as well as by identifying and confirming novel therapeutic target candidates and modulators within a specific cancer context. Evaluation criteria will include the number of publications and citations; the adoption of Network results, methods, and tools by academia and industry; and the number of validated probes or targets.

**Subcommittee Review.** Dr. Martine F. Roussel (Sherr), St. Jude Children's Research's Endowed Chair in Molecular Oncogenesis, St. Jude Children's Research Hospital, voiced the Subcommittee's support for a one-time reissuance of the CTD<sup>2</sup> initiative, which addresses major challenges of precision medicine in oncology by allowing scientists to explore how to bring new technologies in precision medicine to patients. The Subcommittee recognized both the CTD<sup>2</sup>'s efforts to leverage and functionalize TCGA data into a screening network and its impact, as evidenced in the accelerated development of CRISPR technologies and important publications. In addition, the Subcommittee appreciated the concept's plans for an open competition and data quality monitoring, and it encouraged greater advertisement and broader community access to the Network's tools and resources, standardized and systematic approach to develop a complete database, further consideration of the optimal Network platform, and interaction of CTD<sup>2</sup> CRISPR technologies with NCI's PDX efforts.

The first year's cost is estimated at \$12 M for 10–12 U01 awards, with a total cost of \$60 M for 5 years.

**Motion.** A motion to concur on the Office of the Director's RFA/Cooperative Agreement (Coop. Agr.) entitled "Cancer Target Discovery and Development Network Centers (CTD<sup>2</sup>)" was approved with 23 ayes, 0 nays, and 1 abstention.

## Division of Cancer Control and Population Sciences (DCCPS)

### Surveillance, Epidemiology, and End Results (SEER) Program (Reissue RFP)

Dr. Lynne Penberthy, Associate Director, Surveillance Research Program (SRP), DCCPS, presented a reissue concept for the SEER Program. Dr. Penberthy reminded members that SEER is a national resource that supports research on the diagnosis, treatment, and outcomes of cancer since 1973, covers

30 percent of the U.S. population, and provides the only population-based registries in the United States capturing 32 predictive and prognostic markers. SEER data are the most commonly used data to represent trends over time and are used extensively to support statistical analyses and research, with 4,000 downloads of SEER public-use files annually; 17,000 publications have used SEER data since 1975, and approximately 40,000 manuscripts have referenced SEER data. Dr. Penberthy described the evaluation process for the Program, including individual registry studies for quality improvement and national surveillance studies, SEER\*DMS (data management system) external review, internal review of guidelines to direct data collection, and focus groups on natural language processing, a virtual SEER-linked biorepository, and a virtual pooled registry.

The reissue concept enhances the existing SEER infrastructure by leveraging new methods and linkages through central processes and expanding participating registries. The expanded Program will address cancer surveillance challenges including: complexity of cancer care by tracking recurrence and progression in addition to survival; expanded data characterization of each cancer, including molecular and genetic characterization of cancers; dispersion of cancer diagnosis and treatment across multiple health care providers/locations; and unsustainable manual collection by registrars, as well as changing demographic distribution and an aging population. Priorities include representing data in more clinically relevant categories with better representation of special U.S. populations, automating data capture, expanding outcomes data collection, and expanding the capacity of SEER to support cancer research. Proposed changes including expanding “core” registries and adding registries to support key cancer research activities such as the SEER Linked Virtual Tissue Repository and Virtual Pooled Registry.

**Subcommittee Review.** Dr. Ethan M. Basch, Associate Professor of Medicine, Division of Hematology/Oncology, and Director, Cancer Outcomes Research Program, University of North Carolina at Chapel Hill, expressed the Subcommittee’s enthusiastic support for the concept reissuance and recognition of SEER’s importance for understanding cancer trends in the United States. The Subcommittee lauded the concept’s planned expansion and open competition approach, as well as the transition to promote population science through big data capacity advances by capitalizing on technology and potential data linkages, including genomic, pharmacy, and public and private payer data. The expansion to better reflect the diversity of U.S. cancer patients and changing/shifting demographics and to improve the quality of local cancer registries also was commended. The Subcommittee identified long-term follow-up, collection of long-term outcomes, racial and ethnic representation in the data sets, inclusion of patient-reported data, and quality assurance as key areas in the concept.

**In the discussion, the following points were made:**

- Program staff noted that SEER includes significant numbers of subpopulations within its 30 percent cancer surveillance level to ensure that adequate rates are available for Hispanics, Asian Americans, Asian Pacific Islanders, and other specific population groups.
- Selection of SEER biomarkers for data collection is according to current clinical guidelines.
- Data collection currently is a manual process, and more detailed data and cost savings would result from the use of natural language processing, machine learning, and other automated systems to make data linkages.
- Members encouraged the SEER Program to track the prevalence of cancer patients who have been diagnosed with recurrence and are living with metastatic disease.

The first year’s cost is estimated at \$46.2 M for 14–20 RPG awards, with a total cost of \$500 M for 10 years.

**Motion.** A motion to concur on the reissuance of the DCCPS' reissue RFP entitled "Surveillance, Epidemiology, and End Results (SEER) Program" was approved unanimously.

**VII. ONGOING AND NEW BUSINESS—DR. CHI V. DANG**

Dr. Lowy thanked members and presenters for their participation and comments.

**VIII. ADJOURNMENT—DR. CHI V. DANG**

There being no further business, the 57<sup>th</sup> regular meeting of the BSA was adjourned at 3:38 p.m. on Tuesday, 29 March 2016.

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Date

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Chi V. Dang, M.D.  
Chair, Board of Scientific Advisors

\_\_\_\_\_  
Date

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Paulette S. Gray, Ph.D.  
Executive Secretary, Board of Scientific Advisors