National Cancer Advisory Board (NCAB)
***ad hoc* Subcommittee on Global Cancer Research**

February 10, 2022
11:45 a.m.–12:45 p.m. EST
Virtual Meeting

SUMMARY

Subcommittee Members
Dr. Francis Ali-Osman, Chair
Mr. Lawrence O. Gostin (absent)
Dr. Satish Gopal, Executive Secretary
Dr. Scott W. Hiebert
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Margaret Spitz

Other Participants
Dr. Nilofer Azad, NCAB
Dr. Beth Beadle, Stanford University
Dr. John D. Carpten, NCAB
Dr. Laurence Court, The University of Texas MD Anderson Cancer Center
Dr. David Erickson, Cornell University
Dr. Howard J. Fingert, NCAB
Dr. Paulette S. Gray, NCI
Dr. Amy Heimberger, NCAB
Dr. Thu Nguyen, NCI
Dr. Paul Pearlman, NCI
Mr. Ricardo Rawle, NCI
Dr. Aggrey Semeere, Makerere University, Uganda
Dr. Norman E. Sharpless, NCI
Dr. Hannah Simonds, Stellenbosch University, South Africa
Dr. Susan Thomas Vadaparampil, NCAB
Dr. Ashani Weeraratna, NCAB
Dr. Peter Wirth, NCI
Ms. Joy Wiszneauckas, NCI
Dr. Tamara Korolnek, The Scientific Consulting Group, Inc., Rapporteur

Welcome and Opening Remarks
Dr. Francis Ali-Osman, Margaret Harris and David Silverman Professor of Neuro-Oncology, Professor Emeritus of Neurosurgery, Duke University Medical School

Dr. Francis Ali-Osman, Subcommittee Chair, reminded participants that the NCAB *ad hoc* Subcommittee on Global Cancer Research (Subcommittee) is charged with advising the NCAB and the NCI Director on strategic approaches to enhance the NCI's contribution to global cancer research. This Subcommittee will provide leadership and expertise with the intent of offering input on various initiatives, concepts, and partnerships, as well as provide information to help determine the prioritization of new prospects for the NCI in global cancer research. The Subcommittee also may cite new opportunities in which the NCI can contribute internationally, such as by advancing clinical cancer research, building and bridging technology and research capacity, or promoting training programs. Dr. Ali-Osman welcomed new members to the Subcommittee.

Update on NCI Center for Global Health
Dr. Satish Gopal, Director, Center for Global Health, NCI

Dr. Satish Gopal, Subcommittee Executive Secretary, Director, Center for Global Health (CGH), presented an update on the NCI CGH. He noted the Biden administration's commitment to the Cancer Moonshot℠ initiative and to global health, which both were affirmed in White House statements released on 2 February 2022. He reminded the Subcommittee that the CGH 2021–2025 Strategic Plan was published in 2021, with a focus on prioritizing (rather than merely integrating) cancer control into global health programs. The Strategic Plan involves four primary goal areas for CGH-led programs in low- and middle-income countries (LMICs):

- **supporting innovative, impactful research** that addresses key scientific issues in global cancer control or leverages unique scientific opportunities with global partners
- **supporting cancer research training** that enables equitable, impactful global scientific collaboration
- **disseminating current scientific knowledge** into global cancer control policies
- **promoting partnerships** and engagements with key global partners in global cancer research and control

Support of global cancer research includes efforts to accelerate innovative and context-appropriate technology development for global cancer control. A mainstay of these efforts is the Affordable Cancer Technologies (ACTs) Program, which was reissued in 2021. Dr. Gopal highlighted upcoming events and programs that are likely to take place before the next meeting of the Subcommittee. These events consist of new U01 and U54 global cancer implementation science programs, the expansion of the D43 institutional global research training program, dissemination of the 2021 global oncology survey of NCI-Designated Cancer Centers, the 10th Annual Symposium on Global Cancer Research in March 2022 (which, for the first time, will include an Early-Career Investigator Day), and the 2022 Global Cancer Research and Control Seminar Series.

Discussion

Dr. Ali-Osman noted that engaging with the American Association for Cancer Research (AACR) and the American Cancer Society for the Annual Symposium on Global Cancer Research will be effective, because these organizations are active throughout the world.

In response to a question from Dr. Nilofer Azad about monitoring efforts by cancer centers with global health initiatives that are not funded by the NCI, Dr. Gopal mentioned the biannual survey of such centers. This survey was conducted in 2021 and received a 100 percent response rate. The data presently are being analyzed and will be disseminated in 2022. Previous survey results have been published in the *Journal of Global Oncology* and disseminated to the Subcommittee and such organizations as the AACR, the American Society of Clinical Oncology, and the American Society of Preventive Oncology.

Affordable Cancer Technologies Program Overview
Dr. Paul Pearlman, Program Director and Lead for Global Health Technology Research, CGH, NCI

Dr. Paul Perlman, Program Director and Lead for Global Health Technology Research, CGH, provided an overview of the ACTs Program. The ACTs Program supports affordable and resource-appropriate translational technology research. Investigators must demonstrate the utility of such technologies to improve cancer outcomes in LMIC settings; validation in real-world health settings often leads to further innovations. This trans-NCI program focuses on projects with a working prototype, supporting the adaptation of such devices to cancer-related applications, as well as the optimization and real-world

implementation of these devices. Global health care needs—such as distance to care, limited access to pathology, and knowledge-training gaps—drive opportunities for technology development, which is progressing rapidly in several fields. The ACTs Program leverages new platforms (e.g., artificial intelligence [AI], consumer electronics, handheld computers and cellular phones, microfabrication) that are enabling a new generation of point-of-care technologies (e.g., image analysis tools, advanced biosensors, automated sample preparation, molecular diagnostics, lab-on-a-chip) to address significant needs in LMIC health systems. ACTs investigators are expected to consider the context of end-users and their local health systems (e.g., cost, usability, local supply chains, disease priorities, incorporation into local communities). To date, the ACTs Program has supported three funding opportunity announcements, each comprising seven awards. More than half of the funded projects have involved *in vitro* assays, a third have focused on treatment of precancers or enabling higher-quality cancer treatment, and several projects have focused on portable imaging. Dr. Pearlman highlighted gender and racial diversity of ACTs key personnel and investigators, noting that the ACTs Program requires that LMIC personnel be included as key personnel on grants and that equitable leadership plans are included in grant review criteria. Dr. Pearlman listed select program and grant accomplishments:

- In-country experiences have led to new iterations of devices better suited to local environments.
- ACTs technologies have been extended to other targets.
- Projects have led to subsequent funding and have helped catalyze multinational consortia, extending supported technologies to more cancer sites and settings.
- Several technologies have been licensed for further development.
- Results from ACTs grants have contributed to national and international guidelines.
- ACTs has generated interest and related programs from such partners as the U.S. Department of Energy and U.S. Agency for International Development.

ACTs "companion" funding opportunities include an R21 mechanism in context of the Innovative Molecular Analysis Technologies Program, as well as NCI Small Business Innovation Research (SBIR) and Small Business Technology Transfer funding. A U01 cooperative agreement mechanism was used to approve the ACTs Program when it was reissued in 2021. The first cohort of seven new U01 awards will commence in April 2022, and two subsequent annual issuances are anticipated.

Discussion

In response to a question from Dr. Ali-Osman about the number of applications that have moved on to the commercialization or SBIR stage, Dr. Pearlman answered that the earliest cohort still requires time before moving to the commercial manufacturing stage. At this point, licensing is a better benchmark for success, and several of the technologies have been licensed.

Dr. Margaret Spitz asked for more details regarding the *in vitro* assays and their relevance to LMICs. Dr. Pearlman answered that these assays vary widely in their cancer targets. The assays focus on human papillomavirus diagnostics and cervical cancers, HIV-associated cancers, colorectal cancer screening tools, and the early detection of esophageal cancer. The assays are listed on the ACTs Program website.

Early-Stage Diagnosis of Kaposi's Sarcoma in Limited-Resource Setting Using KS-Detect
Dr. Aggrey Semeere, Physician and Clinical Research Scientist, Infectious Diseases Institute, Makerere University, Uganda

Dr. Aggrey Semeere described point-of care diagnosis of Kaposi's sarcoma (KS) in sub-Saharan Africa. KS is a cancer of endothelial cell origin that primarily affects skin and mucus membranes. KS is caused by the KS-associated herpesvirus (KSHV), which is a necessary but not always sufficient cause of KS. KS prevalence has increased since the onset of the HIV epidemic. KS incidence is high even among individuals with HIV who have normalized immune status; up to 30 percent of KS patients die within

4 months of diagnosis. In resource-rich settings, KS is diagnosed pathologically after biopsy; in sub-Saharan Africa, however, biopsies are rare, and clinical macroscopic visual diagnosis is used far more commonly. In the Strategies to Improve KS Outcomes study in Zimbabwe, only 23 percent of diagnoses evaluated were confirmed by pathology. NCI efforts helped establish a free-of-charge skin punch diagnosis service in Uganda and Kenya, but the turnaround time for these samples was too long to be useful to patients, and diagnostic accuracy often was unacceptable.

A point-of-care diagnostic test for KS was developed, enabling an automated liquid biopsy for KSHV DNA to replace solid-phase pathology. Because 40–80 percent of adults in sub-Saharan Africa are KSHV antibody positive, further testing was required to establish specificity of the assay. In collaboration with a team at Cornell University, KS-Detect technology was developed in response to local user feedback and field experience. Now named the Tiny Isothermal Nucleic acid quantification sYstem (TINY), the technology—which utilizes fluorescent-based detection of KSHV DNA—is able to operate using electric, battery, solar, or thermal energy and is portable, inexpensive, and easy to use. Current testing protocols involve bisection of a 5-millimeter cylindrical punch sample, with one-half of the tissue being used for histopathology and the other half being used for HSHV DNA detection by two parallel methods (i.e., standard quantitative polymerase chain reaction and loop-mediated isothermal amplification in the TINY device). These follow-up studies, which took place in the United States, have confirmed the accuracy and specificity of the TINY device. Evaluation of TINY in sub-Saharan Africa via a multisite network for clinical validation is underway. Dr. Semeere credited multidisciplinary research efforts by a network of dermatologists, pathologists, clinical epidemiologists, and engineers for the progress in this area. He envisioned a future in which automated objective molecular diagnosis for KS is a standard approach in any setting.

Discussion

In response to a question from Dr. Ali-Osman about details regarding the liquid biopsies, Dr. Semeere answered that liquid biopsies could detect KSHV DNA or host-response DNA or RNA. These biopsies still are being developed. Dr. Ali-Osman asked about the readout on the TINY device, and Dr. David Erickson affirmed that the readout is quantitative. He noted that a cutoff point has been determined to diagnose KS.

The Radiation Planning Assistant for Radiation Therapy Planning in LMICs
Dr. Hannah Simonds, Associate Professor and Head, Division of Radiation Oncology, Stellenbosch University, South Africa

Dr. Hannah Simonds described automated radiation treatment planning, a response to the challenge of insufficient radiotherapy resources in Africa. As of March 2020, only half of African countries had access to external beam radiotherapy, and only 40 percent had access to brachytherapy. No country in Africa has the capacity to meet the estimated need of one machine per 250,000 population. Dr. Simonds noted that the bulk of radiotherapy machines in Africa are concentrated in the northern- and southernmost regions of the continent. Another challenge is the lack the trained oncology personnel. Most countries that lack even a single clinical oncologist are found in Africa, and 25 African countries are reliant on one clinical oncologist to provide care for more than 1,000 incident cancers. The shortfall of medical physicists and radiation therapists in Africa numbers in the tens of thousands. The bulk of tasks across the spectrum of radiotherapy have the potential to be automated by AI. Automation of image-scan contouring, treatment planning, and quality control tasks can increase consistency and save time for all health care workers involved. Dr. Simonds noted several challenges associated with automation, including the cost, negative responses from staff, and unique resource requirements.

Dr. Simonds described the radiation planning assistant (RPA), which is designed for scalability and is web based for easy upgrades and maintenance. At present, the RPA has the capacity to generate plans for

more than 100,000 patients annually. The RPA can perform multiple tasks, including contouring of normal tissues and targets and generating high-quality two-dimensional, three-dimensional, and volumetric modulated arc radiotherapy plans. It can automatically perform quality assurance tasks for both contours and plans and can identify potential failures (i.e., flag outliers for user review). The RPA has been developed for multiple cancer sites, approaches, and treatment paradigms, with solutions developed based on local practice. The RPA has been evaluated comprehensively with respect to clinical acceptability testing and has undergone almost 8,000 ratings. Overall, 90–100 percent of RPA-generated contours and plans were acceptable as is or with minor edits. Future plans include a U.S. Food and Drug Administration (FDA) submission for clinical use approval and clinical deployment in South Africa in late 2022. The RPA will be scaled to other LMICs while seeking additional funds and support. Future practical directions include integrating the RPA and other AI approaches into clinical workflows and identifying solutions for centers with variable internet and other infrastructure and sustainability challenges.

Discussion

In response to a question from Dr. Spitz about how many other African countries can support the RPA, Dr. Simonds answered that the RPA group presently is working with other countries to understand what their needs are and how to work around these challenges. She noted vast improvements to infrastructure in continental Africa over the past decade. Dr. Beth Beadle added that many governments and philanthropic organizations have sponsored the purchase of linear accelerators but do not have the personnel to run them. Dr. Simonds noted that lack of personnel is a challenge even in South Africa.

In response to a question from Dr. Ali-Osman, Dr. Simonds remarked that the RPA is pending FDA approval. The plan is for RPA to be deployed in other countries that have the minimum staff necessary to run it. Dr. Laurence Court commented that future plans include implementing the RPA in South Africa in the current year and using South African data to scale the RPA to other countries.

Adjournment

Dr. Ali-Osman expressed appreciation to the CGH for the updates and adjourned the Subcommittee meeting at 12:46 p.m. EST.

Dr. Francis Ali-Osman Chair	Date	Dr. Satish Gopal Executive Secretary	Date