

MEETING SUMMARY
PRESIDENT'S CANCER PANEL
**THE FUTURE OF CANCER RESEARCH: ACCELERATING SCIENTIFIC
INNOVATION**

February 1, 2011
Atlanta, Georgia

OVERVIEW

This meeting was the fourth, and last, in the President's Cancer Panel's (PCP, the Panel) 2010-2011 series, *The Future of Cancer Research: Accelerating Scientific Innovation*. During this meeting, the Panel heard testimony about several novel approaches to research review and funding as well as the value of public-private partnerships in biomedical research.

PARTICIPANTS

President's Cancer Panel

LaSalle D. Leffall, Jr., M.D., F.A.C.S., Chair
Margaret Kripke, Ph.D.

National Cancer Institute (NCI)

Abby Sandler, Ph.D., Executive Secretary, PCP
Gwen Darien, Chair, Director's Consumer Liaison Group

Speakers

Scott Campbell, Ph.D., Executive Director and CEO, Foundation for the National Institutes of Health
E. Melissa Kaime, M.D., Captain, U.S. Navy Medical Corps; Director, Congressionally Directed Medical Research Programs
Donald J. Listwin, Founder and Chairman, Canary Foundation
Chandini E. Portteus, Vice President, Research, Evaluation and Scientific Programs, Medical and Scientific Affairs, Susan G. Komen for the Cure
Howard R. Soule, Ph.D., Executive Vice President and Chief Science Officer, Prostate Cancer Foundation, Senior Fellow, The Milken Institute
William J. Todd, President and CEO, Georgia Cancer Coalition
Yun-Ling Wong, Ph.D., Program Officer, Global Health Discovery, Bill & Melinda Gates Foundation

OPENING REMARKS—LaSALLE D. LEFFALL, JR., M.D., F.A.C.S.

On behalf of the Panel, Dr. Leffall welcomed invited participants and the public to the meeting. He introduced Panel members, provided a brief overview of the history and purpose of the Panel, and described the aims of the current series of meetings. Dr. Leffall also noted that Dr. Michael Goldstein, Co-Chair of the American Society of Clinical Oncology Workforce Advisory Group, was unable to attend the meeting as planned.

PANEL I

MR. DONALD J. LISTWIN:

CANCER EARLY DETECTION

Background

Mr. Listwin is founder and chairman of the Canary Foundation, the nation's only nonprofit organization devoted exclusively to early detection of cancer. A 25-year veteran of the technology industry, Mr. Listwin was CEO of Sana Security and Openwave and was the second-ranked executive at Cisco Systems. Mr. Listwin launched the Canary Foundation as a way to address the imbalance in cancer research—less than 15 percent of research funding goes to early detection. Mr. Listwin serves on the Boards of Directors of GenoLogics Life Sciences Software, Calix, Teradici, the Moffitt Cancer Center Comprehensive Research Center in Melanoma, Stratos Biosciences, and the Listwin Family Foundation. He is on the External Advisory Boards for both the Center for Cancer Nanotechnology Excellence and the Early Neoplasia Detection Center at Stanford University and is a member of the Board of Trustees at the Fred Hutchinson Cancer Research Center.

Key Points

- The Canary Foundation focuses exclusively on early detection of cancer and is developing strategies that utilize both blood biomarkers and molecular imaging. Effective early detection techniques could decrease cancer mortality for the overall population as well as reduce the economic burden associated with cancer management.
- The Canary Foundation research program is multidisciplinary and collaborative and is funded in conjunction with multiple sources, including other foundations, government, and industry.
- The Canary Foundation bases its funding model on that of the Department of Defense (DoD) Defense Advanced Research Projects Agency (DARPA) project that resulted in development of the Internet. DoD wanted to replace its hierarchical communications system, which became inoperable if a single component was disabled, with a highly distributed network that would remain operational in the event that some components were compromised. Two companies were each given \$60 million dollars to develop prototypes of such a system, and one prototype led to the creation of the Internet. The development of this complex communications network was achieved because the challenge was addressed using a “systems approach.” Cancer is among the most complex systems but researchers continue to focus on point solutions to fight this disease, which is a flawed strategy.
- A flaw in the current approach to cancer research is that the majority of funding dollars is spent on late-stage cancers. Cancers detected at advanced stages are far more likely to cause death than those detected when the cancer is confined to the site of origin. The Canary Foundation estimates that only \$1 is spent on early detection and prevention for every \$1,000 spent on late-stage cancer treatment.
- A paper published in *Science* reported that it takes about 25 years for colorectal cancer to develop from its initial stages to metastatic disease. Yet, researchers continue to study the disease at its late stages to inform early detection strategies. Colorectal cancer is a genetically different disease at advanced stages compared with early stages. Research needs to target the early stages of disease and scientists must be given access to the right materials to do this.
- A model was developed based on Surveillance, Epidemiology and End Results (SEER) data to determine the probability of cancer cure by tumor size. For lung cancer, treatment usually begins when the tumor is 20 millimeters in diameter. At this size, the survival rate is about 20 percent. In order to achieve 80 percent survival, lung cancer must be detected and treated when the tumor is 1-2 millimeters in diameter.

- Currently available cancer diagnostics are not generally cost-effective, in part because they can lead to unnecessary surgeries. There needs to be a confirming step (imaging or biopsy) between a diagnostic test and surgery. The Canary Foundation has a three-stage strategy for developing cost-effective diagnostics: identification of high-risk populations, administration of a preliminary blood test, and confirmatory molecular imaging.
- This three-stage strategy is exemplified by Canary Foundation efforts related to ovarian cancer screening. The current approach for ovarian cancer screening involves two steps: measurement of the blood biomarker CA125 and conventional transvaginal ultrasound. This approach is currently being evaluated by NCI's Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. The Canary Foundation is comparing this approach with two other strategies: (1) CA125 measurement and molecular ultrasound and (2) measurement of next-generation blood biomarkers (novel blood biomarker panel) and molecular ultrasound. Simulated results of these screening modalities show a reduction in ovarian cancer mortality of 5 percent with CA125 and conventional ultrasound, 16 percent with CA125 and molecular ultrasound, and 25 percent with the blood biomarker panel and molecular ultrasound.
- The current ovarian cancer screening approach is not cost-effective for the general population; however, with a better blood test and the use of molecular ultrasound, screening could become more cost-effective, even for low-risk populations.
- Researchers at Stanford University have built a magneto-nano sensor array that is 1,000 times more sensitive than an enzyme-linked immunosorbent assay and is able to measure 64 different molecules simultaneously. This technology has the potential to aid in the earlier detection of tumors.

DR. YUN-LING WONG:

ONE GREAT IDEA

Background

Dr. Wong received her Ph.D. from the Harvard School of Public Health. Her doctoral work entailed developing an inhaled vaccine for tuberculosis. She has been published in peer-reviewed journals, including the *Proceedings of the National Academy of Sciences*, and featured in *Newsweek*. Dr. Wong is a Program Officer on the Global Health Discovery team at the Bill & Melinda Gates Foundation. Dr. Wong leads the Grand Challenges Explorations (GCE) program, which is counted as one of the most successful programs for discovering and fostering new ideas in the field of health research for solutions to problems in the developing world.

Key Points

- The Bill & Melinda Gates Foundation is organized into three main program areas: Global Health, Global Development, and the United States Program. The Global Health Program focuses on ways to fight and prevent infectious diseases, such as HIV/AIDS, malaria, pneumonia, and tuberculosis, in developing countries. The mission of the Global Development Program is to increase opportunities for people in developing countries to overcome hunger and poverty. The United States Program helps to ensure greater opportunity for all Americans through the attainment of secondary and postsecondary education with genuine economic value.
- The Grand Challenges in Global Health initiative is focused on engaging creative minds to work on scientific and technological breakthroughs for the world's most pressing health problems. GCE is a grant program within the initiative that fosters innovative, early-stage research to expand the pipeline of ideas that may lead to much-needed global health solutions.
- GCE is based on three basic tenets: low burden of entry, champion-based review, and an open path to success. The low burden of entry is facilitated in part by the fact that grant applications are

anonymous—they cannot include indicators of an applicant’s background, experience, or qualifications. Anonymity was built into the application process so that innovative ideas would be considered equally, regardless of the applicant’s expertise or career stage.

- With a champion-based review, each reviewer has the ability to choose one proposal that will automatically receive funding; reviewers can also recommend additional applications for funding consideration. Disagreement can occur among reviewers about the merit of an idea; however, this approach results in a diverse, high-risk portfolio with projects that may “fail spectacularly” or exceed reviewers’ greatest expectations.
- An example of a successful innovative application for global health is the invisible mosquito net to combat malaria. An astrophysicist from Columbia University applied a technology he developed for looking across dust particles in space to develop the virtual net. The invisible mosquito net is composed of infrared light, which blocks the short-range navigation of mosquitos. This idea might have never come to fruition if it were not for the champion-based review process.
- The open-path-to-success tenet refers to the fact that the Gates Foundation will provide support and funding for an idea at the early stages and, then, if warranted, for subsequent steps in the development process. Grantees are responsible for contacting the GCE when they are in need of subsequent funding, which empowers the innovator to drive the research agenda forward.
- GCE is in its second year of funding. To date, 20,000 applications from over 130 countries have been received, and 432 grants (\$43.2 million) have been awarded in 35 countries. Every six months there is a rolling call for proposals. The proposal topics vary depending on recent gaps that have been identified in the global health and development fields.
- The grant application process builds its own momentum. Innovators may propose an idea for one topic that is actually a better fit for a second or third topic, thus facilitating a steady stream of proposals for each grant application topic. Past topics have included: Poliovirus Endgame, Cure HIV Infection, and Low-Cost Cell Phone Applications.
- GCE has found that providing an open path to success and creating a low barrier of entry are critical for encouraging innovative people and ideas to enter the global health and development research realm.

DR. E. MELISSA KAIME:

HOW THE CDMRP ACCELERATES SCIENTIFIC INNOVATION

Background

Dr. Kaime joined the Congressionally Directed Medical Research Programs (CDMRP) staff in June 2005 as Deputy Director, overseeing the day-to-day operations of the program. She became Director of the CDMRP in July 2008. She came to CDMRP after 15 years of service at the Naval Medical Center, San Diego (NMCS), where she was Director of the Breast Health Center and a staff physician in the Division of Hematology/Oncology. She served in Operation Iraqi Freedom II, providing trauma care for coalition forces, insurgents, and civilians in Al Asad and Fallujah, Iraq, from August 2004 to March 2005. Captain Kaime completed a B.S. in engineering from Vanderbilt University, graduating in three years with magna cum laude honors. She earned her M.D. from St. Louis University School of Medicine and then completed her internship and internal medicine residency at the Naval Hospital in Oakland, California, and a hematology/oncology fellowship at NMCS.

Key Points

- CDMRP resides within the U.S. Army Medical Research and Materiel Command and is the second-largest research funding source for breast, prostate, and ovarian cancers.

- CDMRP was created in response to efforts of breast cancer advocacy organizations seeking novel approaches to fund innovative, potentially high-impact research. DoD was chosen to administer the congressionally mandated funding because of its history of medical research and flexible administrative structure.
- CDMRP focuses on high-risk/high-gain research and provides opportunities for investigators to produce preliminary data needed for further funding. Two important aspects of CDMRP are the focus on innovation and the involvement of consumer advocates (i.e., survivors, family members, and caregivers affected by the disease being studied).
- Since its creation in 1992, CDMRP has received over 75,000 proposals and funded nearly 11,000 grants; 14,000 proposals were received in fiscal year 2009 alone. On average, CDMRP funds 10 percent of the applications it receives.
- CDMRP holds investigator meetings at which all program grantees report their results, both positive and negative. It is important to report research results to stakeholders, even if the findings are negative, since knowledge is gained through these so-called failures.
- The purpose of CDMRP is not to compete with other large funding agencies, such as NIH, but to complement them. CDMRP targets critical research gaps and makes efforts to focus its funding on areas that are underrepresented and underfunded. The Programs also focus on innovative research—they take risks on novel hypotheses and support visionary individuals. Some CDMRP award mechanisms—for example, Concept Awards, Idea Development Awards, and Hypothesis Development Awards—specifically solicit innovation. These are typically small awards that range from \$35,000 to \$150,000 over a 12- to 18-month time period. Reviews are focused on the scientific hypotheses since proposals do not require preliminary data and reviews are blinded.
- The CDMRP Integration Panels (IPs), which comprise visionary scientists, clinicians, and consumers, set the Programs’ annual investment strategies and, during programmatic reviews of proposals, make funding recommendations to support those strategies. The IP for each research program defines the focus of research efforts in response to dynamic changes in each respective field. This process allows rapid response to changing needs and implementation of funding mechanisms that are crafted to target those needs.
- Consumer advocates are full partners to the scientists and clinicians on the IPs and are key to pushing innovative ideas forward. The consumers ask questions the scientists might not ask and are constant reminders that the primary goal is to improve the lives of patients.
- For example, a Concept Award that was funded in 2004 to develop methods to visualize circulating breast tumor cells *in vivo* led to discovery of tubulin microtentacles on cancer cells, which attach to the endothelium and invade normal tissue. The two scientists on the IP who reviewed this Concept Award application gave the idea only a “very good” score (the scale is very good, excellent, outstanding); however, the consumer advocate thought the idea was amazing and her enthusiasm resulted in the award being funded. In 2010, the same Concept Award grantee was given an Era of Hope Scholar Award (\$2.5 million) to assemble a multidisciplinary team in a physics-based approach to further develop this innovative idea.
- The Prostate Cancer Clinical Trials Consortium (PCCTC)—which is supported by CDMRP and the Prostate Cancer Foundation—was developed as a way to hasten the development of better therapies for patients through faster and more efficient clinical testing. Scientists and clinicians from the PCCTC member organizations collaborate to design, implement, and complete Phase I and Phase II trials in prostate cancer. PCCTC has not only met the initial goals established by the CDMRP award mechanism, but has laid the groundwork to define common clinical standards in the field of prostate cancer.

- CDMRP has also encouraged innovation by supporting visionary thinkers. Funding of Innovator Awards, which provide investigators with \$5 million over a period of up to five years, is based on general creative ability rather than a specific research plan, and proposals are evaluated based on personal interviews.

DR. SCOTT CAMPBELL:

ACCELERATING CANCER DRUG DEVELOPMENT WITH BIOMARKERS, PERSONALIZED MEDICINE, AND PUBLIC-PRIVATE PARTNERSHIPS

Background

Dr. Campbell is Executive Director and CEO of the Foundation for the National Institutes of Health (FNIH). He received his Ph.D. in basic biomedical sciences in 1985 from the University of South Florida. Following postdoctoral training in cardiovascular physiology at the University of Ottawa in Canada, he spent 12 years in academia at the Michael Reese Hospital in Chicago, the University of Missouri, and the University of South Dakota, where his primary areas of research interest were hypertension, heart failure, and the renin-angiotensin system. Following his academic career and prior to joining FNIH, Dr. Campbell served as National Vice President of Research Programs at the American Diabetes Association (ADA) from 2001-2010. In addition to overseeing all research-related programs at ADA, he was also responsible for helping acquire major donations to the ADA Research Foundation. He had primary responsibility for oversight of the ADA Research Grant Review Committee, Research Policy Committee, and Scientific and Healthcare Council. Internationally, Dr. Campbell was the ADA Research Program liaison to the European Association for the Study of Diabetes and the International Diabetes Federation.

Key Points

- FNIH is the sole organization authorized by Congress to support the mission of the NIH by creating and managing public-private partnerships. FNIH is a nongovernmental organization with an independent Board of Directors; the NIH Director and the U.S. Food and Drug Administration (FDA) Commissioner act as ex-officio Board members. This 501(c)(3) nonprofit organization has raised over \$560 million in the past 15 years in support of over 400 projects. There are currently over 100 active programs, including major research partnerships, scientific education/training, conferences, and facilities.
- FNIH creates innovative public-private biomedical partnerships that complement NIH priorities and advance public health. It provides a neutral forum for bringing partners together. The Foundation uses a structure that enables efficient, effective collaborations and flexible donor relationships. The Foundation has received a four-star Charity Navigator rating for the past four years and is ranked among the top ten charities in the area of medical research.
- The majority of FNIH funding comes from the Bill & Melinda Gates Foundation and the pharmaceutical industry. The Gates Foundation Grand Challenges in Global Health Program has provided over \$200 million in funding.
- Some initiatives with which FNIH is currently involved include the Alzheimer's Disease Neuroimaging Initiative, for which the Foundation has raised \$48 million; the Observational Medical Outcomes Partnership, for which \$25 million has been raised; and The Biomarkers Consortium, for which \$40 million has been raised.
- The Biomarkers Consortium was launched in 2006 to identify, develop, and qualify biological markers to support new drug development, preventive medicine, and medical diagnostics. There is broad participation from stakeholders across the health enterprise—government, the pharmaceutical industry, academia, patient advocacy, and other nonprofit private-sector organizations. The consortium was founded by FNIH, along with NIH, FDA, the Pharmaceutical Research and

Manufacturers of America, the Centers for Medicare and Medicaid Services (CMS), and the Biotechnology Industry Organization.

- The Biomarkers Consortium has 62 contributing members, which include 28 companies and 34 nonprofit organizations, advocacy groups, and trade associations. To date, 13 projects have been approved and 10 have been launched. It is of particular importance that all biomarkers associated with an approved project be qualified by the FDA.
- The goals of The Biomarkers Consortium are to use new and existing technologies to develop and validate biomarkers for specific applications in diagnosing disease, predicting therapeutic response, or improving clinical practice. The Consortium is also focused on generating information to inform regulatory decision-making and making consortium project results broadly available to the entire scientific community.
- The Consortium is governed by an Executive Committee, which includes representation from NIH, FDA, CMS, industry, the general public, and FNIH. The Consortium is focused on four disease areas (cancer, metabolic disorders, neuroscience, and inflammation and immunity), each of which has its own Steering Committee. The Steering Committees usually have both NIH and industry representation and screen all relevant project ideas.
- One area of focus in the cancer arena is fluorodeoxyglucose injection (FDG)-positron emission tomography (PET), which is being evaluated in both lung cancer and lymphoma. FDG-PET exploits the reliance of tumor cells on glucose and glycolytic metabolism to image cancers. FDG-PET is approved for use in diagnosis, staging, and restaging of a variety of cancer types, but has not yet been approved for biomarker usage. FDG-PET can provide an early measure of response to treatment with approved therapies in a number of clinical settings. With a few additional studies, FDG-PET could facilitate both drug development and patient care by helping define and monitor response to chemotherapy and facilitating shorter-duration Phase II studies, which should accelerate testing in Phase III trials and drug approval. Additionally, better patient care will result by identifying ineffective therapies earlier.
- The decision to examine FDG-PET in lung cancer and lymphoma was made because both of these cancers have unmet medical needs requiring new drugs or therapies, and there are existing clinical FDG-PET data for diagnosis and staging for both of these diseases. In lung cancer, there are existing retrospective data on early response. In lymphoma, there are established treatment response criteria that can be refined by FDG-PET.
- To date, 70 non-small cell lung cancer patients have enrolled in the lung FDG-PET study, and 61 patients have enrolled in the lymphoma study. By the fourth quarter of 2010, the lymphoma study had completed 24 months of follow-up in 31 patients.
- The interim goals for these studies are to: evaluate image analysis methods and develop consensus standards for use in clinical trials; coordinate efforts with the Radiological Society of North America through the Quantitative Biomarker Alliance initiative, in consult with the FDA; and prepare initial briefing documents for consideration by the FDA Biomarker Qualification Review Team.
- There are benefits for all stakeholders involved in the FDG-PET studies. Patients will benefit from the availability of better clinical data, which should result in more effective treatment and disease management. The FDA will receive the necessary information for evidence-based regulatory policy. The pharmaceutical industry will have a more efficient drug development and approval path and better early-response criteria. There will be a larger market for PET/computerized tomography (CT) and PET/magnetic resonance imaging (MRI) scanners for the device industry. Study data will help CMS determine whether FDG-PET should be considered part of “reasonable and necessary” care.
- The current development model for an FDA-approved drug takes 10 to 15 years, 1,000-6,000 patient volunteers, and approximately \$1 billion. Inefficient clinical trials account for a majority of the time and cost associated with the failures of this drug development system. An FNIH-supported biomarker

project aims to implement a more efficient clinical trial process. The more efficient process would reduce time to conclusive results, reduce the number of required patients, reduce the cost of conducting trials, and increase collaboration and data sharing.

- FNIH is the sole funder of the I-SPY 2 trial, which builds on the prior, NCI-funded I-SPY1 trial. The I-SPY 2 TRIAL (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And moLecular Analysis 2) is a clinical trial for women with newly diagnosed, locally advanced breast cancer to test whether, prior to surgery, adding investigational drugs to standard chemotherapy is better than standard chemotherapy alone. The I-SPY 2 adaptive trial design will stratify patients into two arms based on HER2 receptor status. Patients will receive standard treatment along with new experimental agents. In regard to trial design, five critical, innovative components are being implemented that have the capacity to change how future clinical trials are designed: neoadjuvant setting; adaptive trial design; molecular and imaging biomarker guidance; testing of multiple drugs simultaneously; and efficient organizational structures.
- I-SPY 2 is being conducted as a large-scale public-private partnership with many stakeholders coordinated by FNIH. These stakeholders include the National Cancer Institute and the FDA as well as multiple pharmaceutical companies, laboratories, nonprofit organizations, and academic institutions. The lead institutions are the University of California, San Francisco and The University of Texas MD Anderson Cancer Center.
- FNIH plays multiple roles in the management of I-SPY 2. FNIH holds the master Investigational New Drug (IND) application with the FDA, manages projects, and negotiates and holds contracts with trial sites, pharmaceutical companies, biomarker companies, and other entities. FNIH also serves as a trusted third party to manage data and intellectual property generated by the trial to maximize public health benefit.
- Researchers hope I-SPY 2 will improve outcomes for the highest-risk breast cancer patients and establish the general value of biomarkers, as well as illustrate the utility of the specific cancer biomarkers used in the trial. It is also hoped that the trial will demonstrate how adaptive design can streamline clinical trials. In addition, future studies should benefit from the work that I-SPY 2 investigators have done with the FDA to develop appropriate regulatory pathways for adaptive trials. I-SPY 2 may also provide a model for collaboration among scientists from academic medical centers, government, and industry.
- It is expected that I-SPY 2 will help generate biomarker profiles that will help predict and/or monitor the effectiveness of each of the investigational drugs included in the trial. Agents will be able to move to smaller, more focused Phase III trials, resulting in lower costs, fewer patients, and an accelerated regulatory process. Results with different agents will provide insight into which molecular signaling pathways are most amenable to intervention. Breast cancer science will move toward the personalized medicine era, with targeted treatments for tumors with different molecular profiles.
- The work of FNIH exemplifies the ability of public-private partnerships to expedite needed changes in cancer clinical trials. These changes include advancing the consensus needed for regulatory science, making data broadly available, sharing intellectual property, qualifying biomarkers, promoting personalized medicine, and testing novel clinical trial designs.

MR. WILLIAM J. TODD:

THE GEORGIA CANCER COALITION: AN INNOVATIVE MODEL, A NATIONAL EXAMPLE

Background

Mr. Todd has been President and CEO of the Georgia Cancer Coalition (GCC) since 2003. Mr. Todd's 39-year career has focused on health care and technology management in Atlanta, Georgia. He was the founding President of the Georgia Research Alliance, which was established in 1990 and has helped build Georgia's reputation as a center for discovery and invention and fostered major advances in science, medicine, and technology. He founded Encina Technology Ventures in 2000. His career began at Emory University hospitals, clinics, and the medical school, where he held a variety of administrative posts over two decades, ultimately serving as Assistant Vice President for Medical Administration at the Robert W. Woodruff Health Sciences Center. Mr. Todd is a graduate of the College of Management at Georgia Institute of Technology and attended the Institute for Educational Management at Harvard University.

Key Points

- GCC is an independent, nonprofit organization that unites government agencies, academic institutions, civic groups, advocacy groups, corporations, and health care organizations to strengthen cancer prevention, early detection and screening, diagnosis, and treatment. GCC was created in 2001 by Hamilton Jordan and Georgia Governor Roy Barnes and was funded primarily by tobacco settlement funds.
- The mission of GCC is to reduce the number of cancer-related deaths in Georgia. The cornerstone of realizing this mission was to recruit and retain world-class cancer clinicians and scientists—referred to as Distinguished Cancer Clinicians and Scientists (DCCS)—to Georgia to strengthen the state's research talent, capacity, and infrastructure. By 2010, 158 scholars were recruited, which exceeded the original GCC goal of 150. GCC provides three levels of funding for these scholars, ranging from \$50,000 to \$150,000 per year for five years.
- GCC helped initiate the first NCI-designated Cancer Center in Georgia—the Winship Cancer Institute of Emory University. The DCCS scholar fund was a key component in developing the research necessary for NCI designation.
- As the DCCS effort has matured, some of these cancer scholars have joined community cancer centers throughout Georgia, including centers in Albany, Savannah, and Decatur. These scholars are working in the community to translate science from the bench to the bedside more quickly.
- The DCCS program has a 6-to-1 return on investment; for every state dollar put into the program, GCC requires at least one private dollar and one Federal dollar. The Coalition has received over \$300 million in Federal and private funding to date. However, there is a need for even greater collaboration and coordination. The GCC would like to support models for funding high-risk, high-priority research, such as the model followed by the CDC Foundation. The CDC Foundation helps CDC pursue innovative ideas that need support from outside partners.
- One of GCC's most ambitious goals is to establish a statewide clinical trials network. It is hoped that the state's cancer clinical trial participation rate will increase with implementation of Georgia's new multispecialty statewide research network, which comprises 186 academic and community oncologists, 57 research sites, 26 cities, and 360 adult clinical trials.
- GCC also has a biorepository initiative—the BioRepository Alliance of Georgia for Oncology (BRAG-Onc). BRAG-Onc was developed to establish a human tissue and tumor sample repository available to investigators throughout Georgia to build upon. BRAG-Onc will also expand biomarker facilities and expertise in the state.

- In 2005, the Institute of Medicine (IOM) released a report on cancer care quality measures used in Georgia. The report contained 52 quality measures developed by an independent panel of scientific experts for the purposes of gauging Georgia’s progress in improving the quality of cancer care and identifying benchmarks for achieving the goals of the GCC. GCC has been using the recommended metrics in the report since 2005.
- The IOM’s 52 quality measures across the continuum of cancer care are used to inform Georgia’s Comprehensive Cancer Control Plan, which is a program of the Centers for Disease Control and Prevention (CDC). The GCC manages this state cancer plan.
- GCC is also involved with the NCI Community Cancer Centers Program (NCCCCP), which is an initiative to develop a national network of hospital-based community cancer centers. All of the program pillars of the NCCCCP are found in the Georgia community cancer centers, including reducing health care disparities, increasing patient participation in clinical trials, supporting high-quality biorepositories, improving the quality of cancer care, expanding the use of electronic health records, and enhancing survivorship and palliative care services.
- GCC is focused on four strategic themes: building stronger bridges between academic medical centers and local communities; maximizing financial leverage; limiting the migration of cancer patients from Georgia’s hospitals to cancer centers in other states; and capitalizing on the advantage of major local players.
- Involvement in the NCCCCP has strengthened bonds between the academic medical centers and community cancer centers in the state. Georgia has two NCCCCP sites: St. Joseph's/Candler's Nancy N. and J.C. Lewis Cancer & Research Pavilion in Savannah; and Northside Hospital in Atlanta. Additionally, the DCCS scholars around the state are a critical link between academic centers and communities.
- “Out-migration” of Georgia’s cancer patients for care is burdensome for some patients and families and results in an economic cost to the state. The Coalition is working to address migration by increasing awareness of state programs and activities. GCC wants to provide better-quality care and better access to care close to home.
- The Coalition has the opportunity to leverage its geographic proximity to key partners in the National Cancer Program, such as the American Cancer Society (ACS) and CDC. GCC seeks to become a test bed for innovative new programs created by ACS and CDC. The states can serve as reliable partners in creating opportunities to increase collaboration and coordination in the National Cancer Program.

DISCUSSION AND CONCLUDING COMMENTS:

PANEL I

Key Points

- It would be beneficial to look across the portfolios of all organizations funding cancer research to comprehensively identify gaps and overlapping areas. Some organizations make the details of their research portfolios publicly available, but not all do. In addition, there is not a central resource for tracking cancer research.
- C-Change, an organization that assembles key cancer leaders from different sectors, may be an appropriate body to evaluate the agendas of the various cancer research organizations and develop consensus regarding an overarching strategy for the National Cancer Program.
- Pharmaceutical companies are now more willing to share data and make compromises in intellectual property negotiations than they have been in the past. These issues are rarely a barrier to partnerships, although discussions are still needed to establish agreements in these areas. Pharmaceutical

companies increasingly realize that they cannot complete the drug development pipeline themselves and recognize the need to work with other stakeholders.

- NIH and NCI have made efforts to revamp their grant review processes in recent years and have implemented many of the concepts that have long been in place within CDMRP. CDMRP has a smaller research program than NCI, which allows it to more easily test innovative approaches to research administration. Larger organizations like NCI can learn from these efforts.
- Addressing health disparities in cancer is an area of focus for CDMRP. Of the cancers that CDMRP includes in its portfolio, prostate cancer has the most dramatic racial disparities in disease outcomes. CDMRP launched a study in 2004 to examine differences among African Americans and Caucasians with prostate cancer in North Carolina and Louisiana. Among African Americans, men in North Carolina have the highest prostate cancer mortality rates while those in Louisiana have the lowest. This study should enable researchers to identify factors (e.g., diet, access to care) that contribute to differences in prostate cancer outcomes between and among racial populations. Upon approval, the data and tissue collected through the project can be accessed by other researchers with relevant research questions.
- Although it is possible to identify examples of successful innovation—such as the Prostate Cancer Clinical Trials Consortium—it is difficult to measure innovation across an entire portfolio. The Integration Panels help ensure that highly innovative projects are represented within CDMRP’s portfolio. Proposals with high scientific merit are often rejected if they do not demonstrate sufficient innovation. This is one way in which CDMRP works to complement the larger research portfolio of NIH, which is more likely to fund incremental research.
- The Gates Foundation uses several criteria to measure the short-term impact of its research investments. The fact that about 15 percent of the Foundation’s awards have been made to developing countries and the high representation of junior faculty members among the grantees indicate that the review and funding process is successfully engaging traditionally underrepresented arms of the research community. The Foundation also tracks the publication trends of its funded investigators to determine whether funding from the Foundation changes the trajectory of these publications. For example, Dr. Marks, the astrophysicist, had previously published only in cosmology journals but recently published his first paper on malaria.
- The Gates Foundation hopes to make 1,000 awards at the level of \$100,000; it will consider its experiment successful if one of these awards achieves its objectives with regard to public health.
- Many investigators are resistant to the concept of blinded review. Some even identify themselves within their proposals. The Gates Foundation does not consider applications in which investigators are identified or those that include preliminary data.
- It seems likely that a blended approach is needed to fund research in public health. It is important to create review mechanisms that facilitate innovation and encourage participation by diverse investigators, including young investigators and those from countries or institutions with less-developed research infrastructures. However, once there is evidence that an idea should be pursued on a larger scale, it may be necessary to build a team of researchers with specific expertise to do the next phase of work.
- The Canary Foundation carefully selects investigators to form teams with the scientific expertise needed to address a problem of interest and then actively manage the teams to ensure that they continue to work toward the desired clinical objectives. Initially, Dr. Lee Hartwell from the Fred Hutchinson Cancer Research Center took the lead in assembling teams, but Mr. Listwin has taken on this role in more recent years.
- Solutions for many of the complex problems facing the cancer research community could likely be found if existing knowledge, expertise, and technology were brought together in a focused way to achieve a specific end goal.

- The ultimate outcome of cancer research is benefit to patients, but this is very difficult to measure, particularly in the short term. Cancer death rates have been declining in the United States for several years but it is difficult to identify the factors that have contributed to this trend. For specific technologies or areas of research (e.g., early detection of ovarian cancer), the desired outcomes are more concrete and can be more easily studied. When evaluating returns on investment, it is important to measure results, not merely effort.
- Innovation can be hindered if organizations or researchers are focused more on sustaining themselves than on achieving specific outcomes. Researchers and funding organizations need to remember that improved public health, not increased funding for their laboratories, should be their primary goal.
- Both consumer advocates and researchers benefit from participating in the CDMRP review process. It is often the first time researchers interact with a person who has been personally affected by the disease they are studying, and this provides them with context and motivation. It is also reassuring to patients to see that there are people working very hard to improve outcomes for those with cancer.
- Insufficient institutional commitment and focus hindered Emory University from gaining status as an NCI-designated Cancer Center, but these factors were eventually overcome.
- Patients with triple-negative breast cancer have worse prognoses than those with most other breast cancer subtypes. The ongoing I-SPY 2 trial is attempting to identify interventions that will improve outcomes for triple-negative patients, but there has not been significant progress in this area to date.
- Early clinical trials in Europe are investigating the use of ultrasound and other techniques that do not involve exposure to high doses of radiation for early detection of cancer, including ovarian and pancreatic cancer. It is hoped that similar trials will be launched soon in the United States.
- Innovative ideas are needed to bridge the gap between observational studies and randomized clinical trials in order to gain regulatory approval for many types of interventions, including preventive interventions. Adaptive clinical trial designs and increased use of biomarkers may help in this regard.
- Partnerships are critical to biomedical research. In developing strategic partnerships, participants should commit to reserving a specific percentage of resources for research and development with the goal of driving innovation. Bringing biologists and engineers together will likely foster innovation and progress and should be encouraged.
- Organizations that fund research—including Federal and state governments and private foundations—should require matching institutional funds for every project funded. This would ensure institutional investment in research.
- There should be open access to the content of journals, particularly reports of research supported with public funds.

PUBLIC COMMENT

Key Points

- Small biotechnology companies are often involved in innovative research and development projects but frequently struggle to secure financing. The NIH Small Business Innovation Research (SBIR) program provides funds for some small business endeavors, but the budget for this program needs to be increased. Many SBIR proposals with high scores do not receive funding. It is also important for academic institutions and investigators to partner with small biotech companies.
- In addition to involving patients in research planning and review, it is important to include community physicians. The vast majority of cancer patients receive their care in community settings and the physicians who treat them can add significant value to research programs. They can provide input on approaches that may not work or be embraced by patients in community settings and can also enhance clinical trial accrual by facilitating access to patients in the community. Efforts also

need to be made to disseminate cutting-edge treatments to the community so that patients receive the best treatment regardless of where they are diagnosed.

- The most important metric of success in biomedical research is impact on patient wellness.

PANEL II

MS. CHANDINI E. PORTTEUS:

SUSAN G. KOMEN FOR THE CURE: RESEARCH TODAY & PROGRESS FOR THE FUTURE

Background

As Vice President of the Research, Evaluation, and Scientific Programs at Susan G. Komen for the Cure, Ms. Portteus is responsible for research grant making, evaluation of mission impact, and oversight of the organization's scientific advisory board and council. Ms. Portteus joined Komen in 2005 as a program manager and became Director of Grants in 2006. In 2010, Portteus became Director of Scientific Programs, overseeing the functions of Komen's scientific advisors, a distinguished group of leaders in breast cancer research who provide expertise across a variety of areas related to the organization's mission. Prior to her work at Komen, Ms. Portteus served as a member of clinical research and public health teams at the University of Texas-Houston School of Public Health, University of Texas Southwestern Medical Center, and Children's Medical Center of Dallas. Ms. Portteus received her Bachelor of Arts in psychology, with a minor in biology, from Austin College in Sherman, Texas, and will receive her Master of Public Health degree from the University of Texas-Houston in spring 2011. Ms. Portteus is a member of the International Cancer Research Partners, the Health Research Alliance Advisory Board, and the American Public Health Association.

Key Points

- Susan G. Komen for the Cure was founded by Nancy Goodman Brinker following the death of her sister from breast cancer. The Komen mission is to save lives and end breast cancer forever by empowering people, ensuring quality care for all, and energizing science to find cures. The organization has a multipronged approach for fulfilling this mission.
- The Komen Affiliate Network is made up of 123 organizations in the United States and Puerto Rico and 2 additional organizations in other countries that work to fulfill the Komen mission within communities. These organizations do not fund research but they do fund education, screening, and treatment programs with money raised through local fundraising. In 2010, Komen provided \$90 million in funding for these activities through its affiliates. Affiliates complete community profiles to assess the needs of the communities in which they reside and invest in initiatives that will address these needs.
- Komen supports health education through its Web site (www.komen.org), helpline (1-800-GO-KOMEN), and development of educational materials.
- The Komen Public and Medical Affairs department handles the foundation's special and strategic partnerships. This department includes the Advocates in Science program, which educates advocates so they can participate in scientific dialogue and make meaningful contributions to the research process.
- Komen is active in public policy at the local, state, and Federal levels. Most recently, the organization has been active in the area of health care reform to help ensure that patients can receive the treatment and screening they need.

- Komen also has several global programs, including the Course for the Cure, an advocacy training program for individuals in countries where knowledge of breast cancer and patient advocacy are limited. The Race for the Cure also takes place in countries other than the United States, most recently in Israel. Komen awards research grants internationally and has several key global initiatives in specific countries. The organization is also working to bring together heads of states and diplomats to bring about improvements in the area of breast cancer advocacy.
- Komen's research program is a crucial part of its mission. The organization funded its first grant in 1982 in the amount of \$28,000. Since that time, the organization has awarded more than \$610 million in support of more than 1,800 research projects. Ninety percent of these funds have been distributed since 2000, illustrating Komen's increased emphasis on research over the past decade. Komen is currently supporting 544 research projects with a total investment of \$273 million.
- Komen raises funds through local fundraising events and the sale of sponsored items. When funds are raised by local affiliates, 75 percent of the money remains in the community while the remaining 25 percent is sent to and managed by the central Komen office for the funding of research.
- In 2007, Komen evaluated and redesigned the focus of its research program. The new strategy focuses on the reduction of breast cancer incidence and mortality of breast cancer within the decade. This represents an increased emphasis on the clinical impact of research rather than solely focusing on scientific merit.
- There has been a significant shift in the focus of the Komen research portfolio over the past three decades. Between 1982 and 1996, approximately 75 percent of the Komen portfolio was focused on biology. While still a significant area of investment, biology comprised only 19 percent of the portfolio in fiscal years 2009 and 2010. Treatment and early detection are now larger areas of focus, representing 31 percent and 24 percent of the portfolio, respectively. Investments in survivorship and prevention have also grown.
- Komen has several types of research grants. Promise Grants support the aggressive translation of scientific discoveries into clinical tools and applications that have the potential to significantly reduce breast cancer incidence and mortality. Projects are generally funded for five years and receive between \$5 million and \$7.6 million. Komen also supports a number of investigator-initiated research projects that explore important issues and novel approaches that will lead to reductions in breast cancer incidence and mortality. Junior faculty are supported through the Career Catalyst Research Program and grants are also available for postdoctoral fellows. Komen also funds post-baccalaureate training grants in disparities research to attract individuals from populations affected by disparities in breast cancer outcomes into careers in science.
- Although overall survival rates for breast cancer have increased in recent years, particularly for those women who are diagnosed at early stages of the disease, there are still a number of complex questions related to breast cancer that need to be answered through research. Komen has identified several such areas—such as triple-negative breast cancer and inflammatory breast cancer—and has awarded Promise Grants in these areas to try to facilitate progress. Promise Grants are expected to result in clinical trials within the funding period of the grant. To date, six of these grants have resulted in the launch of trials and it is expected that 10 more will result in clinical trials within their five-year funding terms. Many Promise Grants are underwritten by other organizations; for example, American Airlines has underwritten a Promise Grant related to inflammatory breast cancer.
- Komen has an intense interest in disparities in outcomes among breast cancer patients. It is known that a number of factors contribute to these disparities but more research is needed in this area.
- Komen recognizes that the availability of genomic data has and will continue to increase. However, more needs to be done to translate these data into clinically meaningful information that supports decision making by patients and providers. It is also important that the research workforce be prepared for the mathematics and bioinformatics questions that will arise in the future.

- Data sharing among cancer researchers is essential. Government agencies and nonprofit organizations should encourage their researchers and grantees to publish all research results, including negative results.
- Organizations should also share tools whenever possible. Public-private partnerships are a good way to drive progress. Collaborations are necessary to address the large, complex issues that are common in the biomedical research realm.
- Komen partners with a number of organizations on various projects. One example is the Susan G. Komen for the Cure Tissue Bank at the Indiana University Simon Cancer Center, which currently is the only bank for normal breast tissue. Komen also partners with the Oncology Nursing Society and the Oncology Nursing Society Foundation to train oncology nurses to educate and support community nurses who interact with cancer patients.

DR. HOWARD R. SOULE:

ACCELERATING THE WORLD'S MOST PROMISING RESEARCH

Background

Dr. Soule coordinates global academic, government, and biopharmaceutical sector research activity and is responsible for the implementation of Prostate Cancer Foundation (PCF, the Foundation) global research strategies. He is also a member of the Department of Defense Prostate Cancer Research Program Integration Panel. In addition, Dr. Soule is a senior fellow of the Milken Institute, a nonpartisan economic think tank and parent organization to FasterCures. Dr. Soule was a senior research and development executive for nine years at Corvas International, Inc., a public biotechnology company, and developed innovative products for the treatment of life-threatening cardiovascular diseases. Dr. Soule received a Ph.D. in virology and epidemiology from Baylor College of Medicine and was a postdoctoral fellow in immunology and vascular biology at the Scripps Research Institute.

Key Points

- Prostate cancer is a terrible disease that affects many men; however, it is less frequently discussed than some other types of cancer.
- There are a number of myths about prostate cancer. Many people think that prostate cancer is a disease that affects only old men; yet, many young men also get prostate cancer. Another common myth is that prostate cancer is slow growing. While it is true that some prostate tumors are slow growing, many types are very aggressive. There is a misperception that prostate cancer is a rare disease, but virtually all men develop prostate cancer if they live long enough. Many men incorrectly believe that they are not at risk of prostate cancer if they do not have family members with the disease; however, only about 10 percent of prostate cancers are hereditary. There are also myths about treatment for prostate cancer. Many people think that treatment always results in impotence and incontinence, but this is not the case.
- Prostate cancer strikes 1 of 6 men in the United States. Rates are higher among African-American men and those with a family history of the disease. In 2010, there were more than 218,000 cases of prostate cancer and 32,000 prostate cancer deaths in the United States. One man dies of prostate cancer every 16.4 minutes in the United States. There are currently more than 2.5 million U.S. men and more than 16 million men worldwide who are living with prostate cancer, making prostate cancer the most common form of non-skin cancer among men.
- There is some evidence that healthy diet and exercise can benefit men who are at risk for or who have been diagnosed with prostate cancer. A recent study found that 90 minutes of walking per week reduced the progression of prostate cancer by over 50 percent.

- There is controversy about prostate-specific antigen (PSA) testing as a screen for prostate cancer. It has been asserted that PSA testing has resulted in unnecessary anxiety and overtreatment; however, it can be an important indicator of the need for further testing. It must be noted that PSA is not a cancer-specific marker and does not distinguish between indolent and highly aggressive disease. PCF recommends that men undergo annual PSA testing but also recognizes the need for better biomarkers for prostate cancer.
- Treatment for early-stage prostate cancer involves prostatectomy, brachytherapy, and/or external radiation therapy. Treatment for more advanced stages of the disease is not as well defined and varies among providers. Approaches include chemotherapy, hormone therapy (androgen deprivation), targeted therapies, and lifestyle interventions.
- PCF was founded in 1993 and is the world's largest philanthropic supporter of research for discovering better treatment and, ultimately, cures for advanced prostate cancer. The Foundation utilizes a venture philanthropy model. To date, it has invested more than \$430 million in prostate cancer research and advocacy. It has funded more than 1,500 projects at nearly 200 institutions in 12 countries around the world. In 2010, the Foundation raised more than \$40 million to support research.
- PCF funds young investigators, who are critical to the future of cancer research. It currently supports 52 young investigators and is hoping to increase that number to 100 within the year. It also supports high-risk ideas not likely to be funded by traditional funding agencies and has funding mechanisms designed to bring together teams of scientists to address complex problems in translational science. The Foundation also supports clinical research through the Prostate Cancer Clinical Trials Consortium (PCCTC, the Consortium).
- There has been a 40 percent reduction in the prostate cancer death rate over the 18 years since PCF was founded. Although this may be due in part to lead-time bias (i.e., men are diagnosed earlier than they would have been in the past), it is also due to improvements in screening and treatment. Although the Foundation does not claim full responsibility, it has played a role in many of the advancements that have contributed to this reduction.
- There were a number of significant advances in prostate cancer research in 2010. Researchers at the University of Michigan identified several genetic fusions with clinical significance in the genomes of prostate cancer cells. In addition, three new drugs for prostate cancer were approved by the FDA. These include Provenge, the first immunotherapy approved by the FDA for treatment of any cancer; the second-generation chemotherapy agent cabazitaxel; and denosumab, a monoclonal antibody against the RANK ligand. PCCTC funded trials of both Provenge and cabazitaxel. PCF-funded researchers also discovered the cell of origin of prostate cancer and developed a model that should be useful as a screening method for new drugs.
- PCCTC began in 1996 when PCF brought together the first six participating centers. The Consortium has a project manager and uses standardized clinical trial agreements and material transfer agreements for all of its trials. It also has a central repository for all data generated through its trials. As of the third quarter of 2010, the Consortium had received 130 letters of intent, of which 103 have been approved for activation. To date, 83 trials have been activated; 48 of these have been completed and 35 are currently open. Consortium trials have enrolled 2,333 men and have resulted in the advancement of eight therapeutic candidates to Phase III clinical trials.
- The Consortium has helped speed the development of a drug called abiraterone, which was discovered by a small company called Cougar. The first trial of this drug started in late 2005 and the Consortium began testing abiraterone in Phase II clinical trials in early 2006. A Phase III trial of the drug was initiated in 2008, even before many of the Phase II trials were completed, because of the promising results. It is likely that the drug will be approved by the FDA in the summer of 2011.

- PCF advocates increased government funding for prostate cancer research in the United States and in other countries around the world. In particular, NCI should partner with PCF and DoD to support PCCTC.

DISCUSSION AND CONCLUDING COMMENTS:

PANEL II

Key Points

- Susan G. Komen for the Cure consults with its scientific advisory board and scientific advisory council to identify the complex questions that are funded through its Promise Grants and other programs. These questions focus on areas in which there has been inadequate progress as well as on disease subtypes and populations for which incidence and mortality are disproportionately high.
- Collaborations among stakeholders are the best way to address pressing and complex questions in cancer research. Komen has partnered in the past with the Love/Avon Army of Women in the area of clinical trials accrual, but the two organizations are not currently working together on any specific projects.
- Komen currently has international affiliates in Germany and Italy, which were established as a result of Ambassador Brinker's relationships with those countries. The organization has sponsored events in other countries (e.g., Egypt, Israel) but feels it needs to gain a more thorough understanding of cultural issues in these regions before establishing additional international affiliates.
- Policymakers have expressed frustration that advocacy groups and foundations do not work together on policy-related issues. There are some organizations that help bring foundations together. One is FasterCures, a nonprofit think tank established by Milken Institute that facilitates collaboration and the sharing of best practices among organizations. Another example is the Health Research Alliance, which fosters collaboration among nonprofit, nongovernmental organizations that fund biomedical research.
- The National Science Foundation recently evaluated one of its team science programs, which focuses on basic science research, and found that teams whose members were geographically dispersed were less productive, on average, than individual investigators or teams within an institution. Komen for the Cure and PCF fund some team science, but the focus is primarily on translational and clinical research. Both organizations have found these investments to be productive.
- Many institutions are using a new technique called intuitive surgical robotic laparoscopy for prostate cancer surgeries. Three laparoscopes are inserted into the patient through small incisions and the surgeon operates the device through a console. This approach is associated with less blood loss, less pain, and shorter hospital stays for patients, compared with traditional surgery. Robotic laparoscopy has not and likely will not be compared with traditional surgery in a randomized trial; although outcomes appear similar at this time, surveillance of long-term recurrence rates following widespread adoption of this technique will be more informative. Many of the most experienced surgeons, who tend to be older, continue to perform traditional surgeries rather than learn the new technique; thus, if patients prefer to receive care from the most experienced surgeons, they may not have the option of having robotic surgery.
- Abiraterone is an experimental antiandrogen treatment for prostate cancer. Currently available antiandrogen drugs or surgical castration are capable of greatly diminishing circulating levels of testosterone and its highly active metabolite dihydroxytestosterone, both of which drive prostate cancer growth; however, low androgen levels persist with these approaches. Abiraterone is capable of reducing androgens to undetectable levels and has resulted in remission in many prostate cancer

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