



Cancer Health Disparities Summit

July 14–16, 2008

Summary Minutes

Cancer Health Disparities Summit 2008: Eliminating Cancer Health Disparities Through Science, Training, and Community

July 14–16, 2008

Bethesda, MD

Center to Reduce Cancer Health Disparities
National Cancer Institute
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Introduction

On July 14–16, 2008, the National Cancer Institute’s (NCI) Center to Reduce Cancer Health Disparities (CRCHD) hosted the annual Cancer Health Disparities Summit at the Bethesda North Marriott Hotel and Conference Center, Bethesda, Maryland. CRCHD is central to NCI’s efforts to reduce the unequal burden of cancer in our society and to train the next generation of competitive researchers in cancer and cancer health disparities research.

The theme of Cancer Health Disparities 2008 was *Eliminating Cancer Health Disparities through Research, Training, and Community*. Summit activities were designed to enhance mutually beneficial interactions among CRCHD programs by sharing scientific knowledge; encouraging junior investigators to network, establish potential collaborations, exchange ideas in order to enhance their career development, and continue in cancer research; and broadening community participation. The Summit’s objectives were to:

- ✓ Highlight scientific achievements across CRCHD research and training programs in basic, clinical, and community-based participatory research.
- ✓ Enhance networking opportunities among colleagues representing cancer and cancer health disparities programs.
- ✓ Familiarize junior investigators with critical components of a successful research proposal and the application review process through participation in a mock review session.
- ✓ Empower community partners to educate scientists and others about culturally appropriate strategies needed to sustain and increase community involvement in research.

Through plenary presentations, concurrent sessions, roundtable discussions, and programmatic meetings, Summit 08 provided more than 900 participants with opportunities to share evidence-based prevention, screening, treatment, and survivorship interventions with their colleagues from a wide spectrum of CRCHD programs:

- ✓ Community Networks Program (CNP)
- ✓ Continuing Umbrella of Research Experiences (CURE)
- ✓ Minority Institution/Cancer Center Partnership (MI/CCP)
- ✓ Patient Navigation Research Program (PNRP).

For the first time, the annual Cancer Health Disparities Summit was combined with the annual CRCHD Professional Development Workshop for junior investigators in cancer and disparities research. Workshop activities were designed to help diversify the cancer health disparities training pipeline. Junior investigators received skills-building information on grant-writing basics and resources for pursuing a successful research career, such as Supplements to Promote Diversity, NRSA (National Research Service Award) F31 Fellowships, and Career Development (K) Awards. A mock review panel gave participants a glimpse into the peer review process. Two judged poster competitions provided junior investigators with an opportunity to showcase their work.

These summary minutes contain highlights of Summit 08 plenary presentations, concurrent sessions, and roundtable discussions. A Final Report, with a complete overview of Summit 08 activities and an evaluation of the Summit’s impact, will be published in the coming months.

Participating CRCHD Programs

Community Networks Program

The Community Networks Program (CNP) is designed to reach communities and populations that experience a disproportionate share of the cancer burden, including African Americans, American Indians/Alaska Natives, Hawaiian Natives and other Pacific Islanders, Asians, Hispanics/Latinos, and underserved rural populations. The overall goal of the program is to engage members of racial/ethnic and underserved communities to become interested and more involved in understanding cancer and to take actions identifying strategies, and research needed to reduce cancer health disparities in their communities. In addition the program is charged with educating and increasing awareness of community members in how to access and utilize beneficial interventions for prevention and early detection of cancer. A critical component of the CNP is to identify and develop a cadre of well trained researchers.

<http://crchd.cancer.gov/cnp/overview.html>

Continuing Umbrella of Research Experiences

The Continuing Umbrella of Research Experiences (CURE) program is a strategic approach for training students and investigators from diverse populations to become competitive cancer researchers. This approach builds on the success of the Research Supplements to Promote Diversity and strategically addresses each level of the biomedical research and educational pipeline to increase the pool of researchers from underserved populations, including racial and ethnic minorities; emphasizes scientific areas of greatest need; and expands and extends the period of training and career development. Funding mechanisms offered through the CRCHD CURE program include the Supplement to Promote Diversity, the NRSA F31 Fellowship, and the Career Development (K) Awards.

<http://minorityopportunities.nci.nih.gov/mTraining/index.html>

Minority Institution/Cancer Center Partnership Program

The objectives of the Minority Institution/Cancer Center Partnerships (MI/CCP) program are to increase participation of minority-serving institutions (MSIs) in the nation's cancer research and research training enterprise; increase the involvement and effectiveness of the Cancer Centers in research and research training and career development related to minorities; and develop more effective research, education, and outreach programs that will have an impact on minority and underserved populations. MI/CCP activities are dedicated to developing stable, long-term, comprehensive partnerships that are mutually beneficial to MSIs and NCI Cancer Centers.

<http://minorityopportunities.nci.nih.gov/institutions/miccp.html>

Patient Navigation Research Program

The overall goal of the Patient Navigation Research Program (PNRP) is to develop effective interventions to reduce cancer health disparities by facilitating timely, continuous access to quality, standard cancer care for all Americans. Patient navigation for cancer care represents a new approach to providing individualized assistance to patients, survivors, and families. Navigation spans the period from cancer-related abnormal findings through diagnostic testing to completion of cancer treatment. Patient navigators are trained, culturally sensitive, health care workers who help individuals address patient access barriers to quality, standard cancer care.

<http://crchd.cancer.gov/pnp/pnpr-index.html>

Monday, July 14, 2008

Welcoming Remarks

Summit 08 Planning Committee Chairs

Ms. Tarsha McCrae, Public Health Analyst, Disparities Research Branch, CRCHD
Ms. Belinda Locke, Program Director, Diversity Training Branch, CRCHD
Dr. Leslie C. Cooper, Program Director and Team Leader of the Community Networks Program, Disparities Research Branch, CRCHD

Ms. McCrae reviewed the Summit 2008 agenda, reminding participants to attend the two poster competitions, visit the exhibitors' tables, and participate in programmatic meetings.

Ms. Locke explained that, as a result of the incorporation of the NCI Comprehensive Minority Biomedical Branch into CRCHD, the Professional Development Workshop formerly sponsored by that Branch has been built into the agenda of Summit 2008.

Dr. Cooper reminded participants that everyone has a role to play in eliminating cancer health disparities. She encouraged interactive involvement in Summit events to increase collaboration within and across CRCHD programs.

Sharing the Vision and Setting the Stage

Sanya A. Springfield, Director, CRCHD

Dr. Springfield noted that the Summit 2008 agenda was designed in response to feedback from previous summits. Participants expressed an interest in presentations highlighting the scientific accomplishments of CRCHD programs and asked for information and activities focused on mentoring junior investigators.

CRCHD Reorganization

CRCHD has been reorganized to focus on two strategies for addressing cancer health disparities. The Disparities Research Branch conducts and supports research across the cancer continuum, from early detection to survivorship and end-of-life issues. The Diversity Training Branch focuses on building a cadre of young investigators by providing support and mentoring throughout their educational experiences and early careers. Both branches are supported within CRCHD by a variety of core resources focusing on communications, planning, and evaluation. Dr. Springfield asked the CRCHD Branch Chiefs, program staff, administrative staff, and interns to stand and be recognized.

Two members of the CRCHD staff were highlighted due to their impending departure. Dr. Roland Garcia, who led the development of the Patient Navigator Program, is retiring; Ms. Belinda Locke, who led the Career Development Program, is moving to the National Institute of Child Health and Human Development. Dr. Springfield encouraged interested individuals to consider applying for one of these positions.

Budget Issues

Cancer health disparities researchers are understandably concerned about the likelihood that they will be able to obtain funding. The number of applications for grants to support investigator-initiated studies is increasing, but the flat National Institutes of Health (NIH) budget has led to decreasing success rates.

Several important cancer health disparities initiatives were approved recently by the NCI's Board of Scientific Advisors (BSA), but in 5 years they will have to be resubmitted and receive close scrutiny from the BSA. Three other initiatives will be submitted for renewal in fiscal year 2009.

Heightened competition within NCI for limited set-aside funds means that programs like those sponsored by CRCHD must be able to clearly demonstrate their value to sustain their progress. To this end, national-level evaluations are less important than individual progress reports that highlight success in cancer health disparities research and training. Dr. Springfield urged participants to attend the Summit 2008 session on evaluation to learn how they can help provide the information needed to show the NCI Executive Committee and BSA how important and productive these programs are. There will also be a session on how to educate local and state decision makers about the importance of programs designed to address cancer health disparities.

New Initiatives

Several new initiatives have been launched. The GMaP concept (Geographical Management of Cancer and Cancer Health Disparities Programs) will use a regional satellite approach by building synergistic “hubs” of researchers and programs committed to strengthening cancer health disparities research and training efforts. In fiscal year 2009, GMaP will be piloted in the DC/Maryland/Virginia region and in California. The Emerging Technology Training Program will also be piloted at two sites. In addition, two R03 solicitations will be issued to provide 3-year grants to young investigators involved in the MI/CCP and CURE programs.

CRCHD, in partnership with the American Association for Cancer Research (AACR), will again cosponsor a meeting on the science of cancer health disparities this year. Another important partner of the CRCHD is the National Center on Minority Health and Health Disparities, which has provided co-funding for the CNP and MI/CCP programs.

Plenary I—Program Snapshots of CRCHD Initiatives

Moderator: Kenneth Chu, Chief, Disparities Research Branch, CRCHD

Community Networks Program

Leslie C. Cooper, Disparities Research Branch, CRCHD

The Community Networks Program (CNP) is one of the key programs within the Center to Reduce Cancer Health Disparities. The purpose of the CNP is to reduce cancer disparities in racial/ethnic minorities and underserved populations by increasing access to and use of beneficial biomedical procedures in primary and secondary prevention and to develop a cadre of well-trained researchers who will continue to reduce disparities in communities. The underlying scientific approach being used is Community-Based Participatory Research (CBPR).

CBPR mandates a partnership between traditionally trained scientists and members of the community, with all parties interested in addressing a common research problem. Community members not only serve to recruit participants to research studies but also play an active role in helping to design the studies, identifying key research questions to be addressed, participating in the development and implementation of the various interventions, data collection, dissemination of findings (going beyond peer-reviewed journals, to include lay publications as well), and sustaining programs beyond the grant funding period.

The framework for the CNP is a planning model that provides guidelines for building program elements, conducting research and training activities, measuring impact (both short- and long-term), and evaluating programs. The CNPs understand that within their 5-year funding period, they will not be able to fully eliminate cancer health disparities; rather, their goals are to build research capacity in the community, increase the number of competitive disparities researchers, and establish sustainability. Each CNP is creating a roadmap for the future elimination of cancer health disparities.

The CNPs primarily focus on breast, cervical, colorectal, and prostate cancers but some also conduct tobacco-related research or research on liver, stomach, or lung cancer. The programs target African-

American, Hispanic/Latino, American Indian/Alaskan Native, Pacific Islanders, Asia-American, and other underserved populations.

All 25 CNPs have initiated Phase I of the program, which involves capacity building and increased cancer education and awareness. Phase I requires the development of partnerships within the community, formal collaborations with other NCI-funded programs, and implementation of community-based primary and secondary cancer prevention activities. All CNPs are in Phase II, which involves conducting disparities research and developing training activities for community members and junior investigators.

Junior/new CNP investigators have begun conducting pilot studies supported by small grants. In 2006, 51 applications for pilot studies were submitted for peer-review, with 15 of these being awarded. Since 2006, 53 CNP pilot study grants have been awarded. Young researchers are being encouraged to move on from the pilot study experience to apply for traditional NIH investigator-initiated grants.

CNPs are also partnering with other Health and Human Services (HHS) agencies to add to their capacity to reduce cancer health disparities through the utilization of beneficial services. The Health Resources and Services Administration (HRSA) has contributed resources for screening through HRSA-based clinics. The Patient Navigation Program in Detroit, supported by the Centers for Medicare and Medicaid Services (CMS), collaborates with the Karmanos Cancer Institute CNP in Detroit by providing cancer screening and treatment to individuals recruited by the CNP. In addition, CMS supports one of the CNP Pilot Studies. The Centers for Disease Control (CDC) provides screening services to eligible community members through its Breast and Cervical Cancer Early Detection Program. In addition, several NIH Institutes have helped CNPs expand their efforts.

Next steps include completing all of the requirements as indicated in the initial RFA, completing local and national evaluations, disseminating information about successful activities within our CNPs and beginning to move towards conducting evidence-based interventions for our targeted populations, expanding efforts to reduce and eliminate disparities, and securing support to continue and expand the CNP.

Minority Serving Institution/Cancer Center Partnership

Nelson Aguila, Diversity Training Branch, CRCHD

The MI/CCP was initiated in 2001 to enable MSIs and Cancer Centers to equitably pool their strengths for mutual benefit. The goals of the program are to build the research capacity of minority-serving institutions; create stable and long-term collaborations in cancer training, cancer research, career development, and outreach between minority-serving institutions and cancer centers; improve the effectiveness of cancer centers in reaching underserved communities; and export this collaborative model(s) to other cancer centers to help them achieve the same objectives.

MI/CCPs have been supported through the P20 (for feasibility studies), U54 (a cooperative comprehensive planning grant), and U56 (cooperative planning grant) funding mechanisms, although the U56 is no longer being used. The next due date for submission of applications for MI/CCP P20 grants is April 15, 2009. The U54 request for applications will also be reissued in 2009.

The basic, clinical, and community-based research projects initiated as a result of MI/CCP collaborations have resulted in the publication of hundreds of high-quality, peer-reviewed journal articles. The success rate of grant proposals derived from MI/CCP projects is a remarkable 56 percent. MI/CCP programs have also served hundreds of trainees from high school through postdoctorate levels and increased the diversity of researchers on the faculties of both MSIs and Cancer Centers. Several MI/CCP junior investigators made presentations at the recent symposium jointly sponsored by CRCHD and AACR.

Next steps for the MI/CCP program include:

- v Increasing publications and grant submissions

- ✓ Evaluating the impact of the MI/CCP program
- ✓ Tracking and evaluating training and educational programs
- ✓ Improving communication among partnerships
- ✓ Increasing outreach and clinical activities
- ✓ Developing new funding mechanisms.

Patient Navigation Research Program

Martha Hare, Disparities Research Branch, CRCHD

Patient navigation for cancer care represents a new approach to providing individualized and culturally appropriate assistance to patients. NCI's Patient Navigation Research Program, established in 2005, is devoted to systematically evaluating the efficacy of patient navigation interventions by linking primary outcome measures to program goals. The primary PNRP outcome measures are improved timeliness of resolution following an abnormal screening finding; improved timeliness of commencement of standard cancer care treatment following any positive cancer diagnosis; improved patient satisfaction with the health care system experience; and cost-effective patient navigator interventions.

As part of its research program, the PNRP tracks common barriers that patients encounter and the actions taken by navigators to help patients overcome those barriers. Barriers may result from cultural differences such as language, individual patient concerns (e.g., finances and transportation), or health care system factors (e.g., lack of health insurance).

Activities often used by patient navigators to reduce barriers that prevent access to care include finding appropriate financial aid; identifying and scheduling appointments; arranging transportation and child care; and providing or arranging translation and interpretation services. They ensure coordination among medical providers and provide patient education.

Nine PNRP sites (eight funded by NCI and one by the American Cancer Society [ACS]) are located throughout the United States. They reach out to communities with the greatest cancer health disparities, including African-American, Hispanic, Native American, Alaska Native, and medically underserved populations. The PNRP focuses on four types of cancer with a large public health impact. All sites navigate patients with breast abnormalities or breast cancer; some also navigate patients with cervical, colorectal, and/or prostate abnormalities or cancer diagnoses.

Patient navigation requires a unique skill set of cultural sensitivity, empathy, and the ability to communicate with health care professionals. In addition, whenever possible, sites seek to match the race or ethnicity of patient navigators with the patients themselves. Patient navigators represent a wide variety of disciplines, including nursing, medical assistance, community health work, health education, and social work. Many people become navigators because of their own experiences with cancer, whether as a survivor, a caregiver, or as an outgrowth of prior professional experience. Because patient navigation requires collaboration between primary care and cancer specialties, navigators must be able to access a wide variety of community resources. Professional development for navigators is accomplished through national, centralized training and ongoing site-specific activities. An annual workshop with American Cancer Society funding is held each year. In addition, patient navigators have access to Web-based continuing education resources.

PNRP sites have leveraged NCI funding to obtain additional support totaling approximately \$10 million. Some of these funds have been used to support site-specific studies and enhance navigation services. PNRP sites have developed approximately 300 partnerships with community organizations, federally funded programs (e.g., the NCI Community Clinical Oncology Program and the Veterans Administration), and community health centers system; they have also established community advisory boards. More than 30 trainees have been mentored by PNRP staff. The program has enrolled more than

3,000 patients, and preliminary data analyses have begun. Instruments for data collection have been designed on the national level and a national Data Analysis Committee oversees development and maintenance of an online program-wide data dictionary with more than 600 core data elements. A logic model has been developed to support national and local program evaluation. Demonstrating the success of PNRP research activities will be a key factor affecting funding decisions when the PNRP is considered for reissuance in the coming year.

Continuing Umbrella of Research Experiences

Belinda Locke, Diversity Training Branch, CRCHD

The Continuing Umbrella of Research Experiences, or CURE, is a strategy to establish, maintain, and nurture a pipeline of trainees on an educational path to become well-trained, competitive cancer investigators. The goals of the CURE are to increase the pool of investigators representative of diverse populations, emphasize scientific areas of greatest need, and expand and extend the period of training and career development. CURE is an important part of one of CRCHD's overall goals, which is to lead NCI's efforts to train students and investigators from diverse populations to be the next generation of competitive researchers in cancer and cancer health disparities research.

The CURE program was initiated in 1996 through Diversity Supplements that supported the training of individuals from diverse populations from high school through the junior investigator level. This program has continued to evolve in response to the changing needs of awardees and gaps identified through portfolio analysis. The CURE Supplements for Cancer Centers P30 grants were added to increase the numbers of high school and undergraduate students supported by the CURE program. Because most of the research being supported through this program focused on basic science, supplements to institutional grants (R25T) were added to support students and trainees from diverse populations involved in population-based research on cancer prevention and control. The Ruth L. Kirschstein National Research Service Award for Individual Predoctoral Fellowships to Promote Diversity in Health-Related Research (F31) was implemented for students enrolled in a doctoral program.

Supplements to Specialized Programs of Research Excellence (SPORE) grants were developed to support translational research. Supplements awarded through the Community Networks Program have resulted in an increase in the number of cancer disparities studies in the NCI research portfolio. New supplements for Cancer Centers have increased patient-oriented research.

Several career development awards in the K award series were put in place to help sustain junior investigators while they collected data necessary to develop their first successful applications for R01s and other investigator-initiated awards. The program is considering implementation of R03 and R21 mechanisms to further extend this career development training period.

The CURE program has created a pipeline of diverse cancer investigators. The program supported over 360 investigators in 2007. Currently, more than 180 individuals are supported by CURE supplements. Approximately 80 ongoing studies are supported through the F31 mechanism. Approximately 60 ongoing studies are supported through career development awards. More than 1,600 publications have been contributed to the scientific literature. More than 50 competitive grants, most of which are R01s, have been obtained by CURE participants. CURE grantees have assumed numerous prominent academic and research positions. Grantees have served on more than 190 committee sessions, which represents approximately 17,000 days of review service. Equally important is the creation of a pipeline of diverse cancer research mentors.

Other Summit 2008 sessions related to the CURE program include two concurrent sessions that feature presentations by junior investigators, a poster competition, and a mock grant review session.

Key Points of Discussion—Plenary I

- v Although NCI cannot formally partner with advocacy groups to conduct lobbying efforts, all NCI grantees and their community partners are encouraged to take advantage of every opportunity to educate decision makers about the importance of sustained funding for cancer health disparities research.
- v Scientists involved in community-based participatory research on cancer often feel that other health problems of their patients should be taken into account. NCI and other NIH Institutes usually devote their limited funds to specific diseases, but co-morbidity is being addressed at the NIH and HHS levels and by the National Center for Minority Health and Health Disparities. Several CNP advisory committees have expanded their concerns beyond cancer to address the needs of the community by developing spin-off groups.
- v The PNRP is only one of numerous national patient navigation programs established in response to the Patient Navigator Outreach and Chronic Disease Prevention Act of 2005.
- v CRCHD programs address not only racial and ethnic populations but the underserved as well. One example is poor, rural whites in Appalachia.
- v An important aim of the CURE program is to teach first-generation students how to develop research training plans. Staff of the Disparities Training Branch work with potential grant applicants on an individual basis, often using copies of successful grant applications (with private information deleted) as a teaching tool.
- v Leaders of medical and academic organizations sometimes lack an understanding of the importance of patient navigation programs within their organizations. Steps should be taken to fully engage these organizations to become involved in the research process.

Plenary II—Biological Determinants of Cancer Health Disparities

Moderator: Belinda Locke, Diversity Training Branch, CRCHD

Impact of BRAF, MLH1 on the Incidence of Microsatellite Instability High Colorectal Cancer in a Population-Based Study

Hassan Brim, Howard University

Population-based studies are conducted to understand the specifics of disease development within particular populations. Dr. Brim's microsatellite instability study provides insight into the contributions of gene variants and gene-environment interactions to colorectal cancer within three populations: African American, Omani, and Iranian.

There are many factors behind the development of colorectal cancer (CRC); this study focuses on the driving force of gene instability (mutations in the gene sequence)—in particular the oncogene BRAF, and the DNA mismatch repair genes MLH1 and MSH2. Oncogenes participate in cell proliferation and mismatch repair genes create a higher rate for mutation if their function is impeded. Patients with microsatellite instability—resulting from inefficient DNA mismatch repair genes—have a lower survival rate than patients with microsatellite-stable tumors. Microsatellites are sections of DNA consisting of repeating units, usually 1-6 base pairs in length. This study sought to identify the proportion of the microsatellite instability phenotype to mutated DNA mismatch repair genes, as well as the correlation to the BRAF mutation.

In the African-American population, the mean age for colon cancer was 65.7 years; most of the tumors were proximal. A majority of the tumors lacked MLH1 expression, probably because 94 percent of these

tumors exhibited methylation of the promoter region of the MLH1 gene. Additionally, 9.7 percent of the patients had a BRAF mutation; tumors from patients with BRAF mutations also tended to exhibit microsatellite instability.

Iranian patients were an average of 60 years old with primarily distal tumors. Rates of BRAF mutation and MLH1 methylation were lower in this group in comparison with the African-American sample. The average age of the Omani patients was much lower at 52 years. There was a predominant methylation of the MLH1 gene, with a high rate of BRAF mutation of about 18-19 percent.

Important results from this study are: the rate of microsatellite instability for African-American patients is 2.54-fold higher than the national average; the BRAF mutation is an important factor in the microsatellite instability tumors for the African-American and Omani patients, but not for the Iranian patients; and the location of tumors is mostly proximal in African-American patients. The implications of this study are important because patients with microsatellite instability generally do not respond to chemotherapy. Future research entails the use of high-throughput technologies to compare data from African Americans with what is already known in the literature with the general population.

Age, Sex Steroids, Inflammation, and Prostate DNA Methylation

Bernard Kwabi-Addo, Howard University

Since the 1970s, there has been a steady rise in prostate cancer in the United States, with the incidence and mortality from this devastating disease appearing two-fold among African-American men. This disparity is due to a combination of environmental, genetic, and socioeconomic risk factors. Other potential risk factors for prostate cancer include sexually transmitted diseases, obesity, smoking, and alcohol abuse.

Studies evaluating genetic links to prostate cancer show the disease has a significantly stronger hereditary component than any other cancer. At the time of diagnosis, prostate cancer cells show multiple somatic changes—including DNA rearrangement, DNA amplification, and epigenetic mutations. One particular mutation, of the androgen receptor, has been identified as directly responsible for the progression of prostate cancer.

The higher susceptibility of African Americans to prostate cancer has also been linked to an elevated frequency of single nucleotide polymorphisms (SNPs). A SNP is a genetic variation that occurs when a single nucleotide (i.e., an adenine, cytosine, thymine, or guanine) is replaced by one of the three other nucleotide types. The most important finding in prostate cancer genetics is the identification of SNPs on chromosome 8Q24. In addition to various genetic mutations, prostate cancer cells also exhibit epigenetic changes that occur much earlier in disease progression than other genetic defects.

A common epigenetic change associated with cancer development is DNA methylation—a process that can lead to silencing of gene expression. The function of methylation is to prevent unwanted transcription of genes. In normal prostate cells the bulk of the genome appears to be methylated, whereas the promoter region is unmethylated. However, in prostate cancer cells the methylation pattern is reversed and the promoter region appears to be more methylated. Normal prostate cells undergo a relentless barrage of genome-damaging stresses; the accumulation of these mutations may prompt changes in methylation patterns, increasing susceptibility to further downstream genetic abnormalities.

Dr. Kwabi-Addo's lab sought to determine whether DNA methylation changes are a function of aging, exposure to carcinogens or sex hormones, or chronic inflammation. Overall, they found a significant increase in methylation as a function of age for several tissue-specific genes. The data confirm that DNA methylation starts in normal prostate tissues, increases as one ages, and becomes abnormally higher in cancer cells. DNA-methylated genes can be used as a candidate biomarker for disease detection—in particular, the Nkx-2.5 gene, which shows about a threefold higher methylation level in the cancer state in comparison to the normal state.

Ongoing studies address the methylation patterns of genes in signaling pathways such as chronic inflammatory pathways and sex steroid and hormone pathways and compare their methylation status in normal versus cancerous tissues. Future studies will focus on the effects of environmental factors on methylation and consider whether such variation can account for disparities in incidence among different ethnic groups.

The Relationship of Her2 Oncogene Overexpression With Survival and Relapse in Native Hawaiian Females With Breast Cancer

Clayton Chong, 'Imi Hale Native Hawaiian Cancer Network

When looking at the five leading ethnic populations in Hawaii, the Native Hawaiian population ranks first in mortality due to cancer in females. In 2005, an analysis of just over 4,500 females was conducted using the Hawaiian tumor registry to observe 5-year cancer survival rates in the Hawaiian population.

Compared with Caucasians, Hawaiians had the poorest 5-year survival, with discrepancies especially apparent in the advanced stages of breast cancer. This disparity in cancer survival led Dr. Chong and his team to question whether an emphasis on screening and early detection would be sufficient enough to improve outcomes or whether the tumor biology of this ethnic group plays a significant role.

In order to determine the role of tumor biology in survival rates, HER2 expression was studied. HER2 is a noninherited proto-oncogene that is normally present in breast cancer, but when overexpressed leads to aggressive cancer progression and poor survival rates. HER2 prevalence was compared between 400 Hawaiians and 565 Caucasians over a 7-year period. There were no differences in HER2 prevalence, but when HER2 was overexpressed in Native Hawaiians the mortality risk doubled and the risk for relapse tripled. Study limitations included a small sample size and an abbreviated length of follow-up; nevertheless, it was concluded that Native Hawaiian women who are HER2-positive have a disproportionate increased risk of relapse and mortality.

Four breast cancer phenotypes are currently being investigated in the literature, and further research is necessary to explain why HER2 expression leads to poor prognosis, especially in Hawaiians. Questions to explore include whether: there are biological reasons for the HER2 disparity; Native Hawaiian women are less responsive to anti-HER2 therapy; and Native Hawaiian women are less likely to receive anti-HER2 therapy?

Key Points of Discussion—Plenary II

- v In order to accurately assess disease disparities among different ethnic populations (e.g., colorectal cancer in African Americans and Iranians), researchers must integrate molecular data with other parameters such as access to health care and aggressiveness of the disease.
- v Currently, the best screening option for prostate cancer is the prostate-specific antigen (PSA) test. Early detection increases the chances of better treatment, but PSA alone may be inefficient in some cases. A better screening standard should be established (e.g., PSA plus digital rectal exams).
- v A promising premise for future HER2 research would be to identify the protein structure of HER2 in Hawaiian women to determine whether structural differences are accountable for unresponsiveness to Herceptin (anti-HER2) treatment.
- v It was also suggested that studies address the obesity rate in Native Hawaiian versus Caucasian women and whether there is a correlation between obesity and HER2 overexpression.

Concurrent Session I-1: Signal Transduction of Cancer (I)

Moderator: Nelson Aguila, Diversity Training Branch, CRCHD

Downregulation of the c-MYC Target Gene, Peroxiredoxin III, Contributes to Arsenic Trioxide-Induced Apoptosis in APL

Pablo Vivas-Mejía, University of Texas M. D. Anderson Cancer Center/University of Puerto Rico Comprehensive Cancer Center

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML), which is more common among Hispanics than other populations. APL accounts for 10 percent of AML cases and is cytogenetically characterized by the translocation of chromosomes 15 and 17. All-trans-retinoic acid (ATRA) and arsenic trioxide (ATO) are used to treat APL patients; both drugs induce differentiation and ATO also induces apoptosis of APL cells. ATO has been investigated in clinical trials for other cancers, and there is evidence that the drug can eliminate cancer initiating stem cells; however, use of the drug has been hampered by safety concerns. Learning more about how ATO induces apoptosis of cancer cells could lead to its safer clinical use or the development of novel drugs that cause apoptosis in APL and other leukemic cells without interfering with other physiological processes.

Peroxiredoxins (Prxs) are a family of antioxidant thioredoxin-dependent enzymes that catalyze the reduction of hydrogen peroxide, peroxynitrite, and organic hydroperoxides. The accumulation of these molecules can alter mitochondrial membrane potential, leading to apoptosis. Prx III is located in the mitochondria of cells and is highly expressed in white blood cells. Expression of Prxs is increased in several human cancers. It is hypothesized that Prx III is a target of ATO and that its inhibition by ATO results in apoptosis of APL cells.

To test this hypothesis, experiments were carried out to determine the effects of ATO treatment or manipulation of Prx III on the human APL cell line NB4. ATO decreased Prx III mRNA and protein levels in NB4 cells in a dose-dependent manner; this downregulation correlated with decreased levels of the transcription factor c-MYC. Subsequently, accumulation of reactive oxygen species was observed and the mitochondrial membrane potential dissipated. After 24 hours of treatment with ATO, apoptosis of NB4 cells increased by 30 percent.

To further study the role of Prx III, Prx III levels were depleted using siRNA technology. NB4 cells with lower levels of Prx III exhibited accumulation of reactive oxygen species, loss of mitochondrial membrane potential, and evidence of mitochondria-dependent apoptosis. All of these effects were enhanced with the addition of ATO. Experiments in which another leukemia cell line was manipulated to overexpress Prx III were carried out to further elucidate the role of this protein in ATO-induced apoptosis. Prx III overexpression resulted in resistance to ATO-mediated apoptosis.

Various experiments were carried out to address the role of c-MYC in ATO-mediated apoptosis. Use of a c-MYC inhibitor and a cell line in which c-MYC expression was knocked down revealed that this transcription factor is responsible for maintaining expression of Prx III. A chromatin immunoprecipitation assay showed that ATO treatment of NB4 cells leads to reduced binding of c-MYC to the canonical E-box in *Prxd-3*, the gene for Prx III.

In summary, these experiments suggest that ATO-induced downregulation of c-MYC leads to subsequent downregulation of Prx III. Decreased levels of Prx III contribute to accumulation of reactive oxygen species and dissipation of the mitochondrial membrane potential, changes which help trigger mitochondrial apoptotic events. These results provide further insight into mechanisms of ATO-mediated apoptosis in APL cells. Future experiments will be conducted using cells retrieved from leukemia patients.

Key Points of Discussion

- v The investigators have not attempted to rescue the ATO-treated cells with antioxidant compounds.
- v There are additional pathways, such as the NF- κ B pathway, through which ATO causes apoptosis.
- v ATO does not induce autophagy in NB4 cells.

The High-Affinity Selectin Glycan Ligand C2-O-sLeX Mediates Adhesion of Human Carcinoma Cells to Vascular Endothelium

Catherine St. Hill, University of Minnesota

Invasion and metastasis of tumor cells are responsible for much of the morbidity and mortality of cancer. Tumor cells somehow enter blood vessels, travel to other sites in the body, and then exit the vasculature to form metastases in new tissue. The role of sialyl Lewis X-modified core 2 O-glycans (C2-O-sLeX) in the adhesion and metastasis of cancer cells is being investigated. Sialyl Lewis X (sLeX) is a terminal glycan structure found on mucin type glycoproteins, including C2-O-sLeX. Two enzymes important for sLeX formation are C2GnT1 and FucT-III. Leukocytes and cancer cells use sLeX as a ligand for binding to selectins (selective lectins), which are found in leukocytes, platelets, and endothelial cells. Several types of cancer, including breast and colon, exhibit increased expression of sLeX, which is associated with poor prognosis. Additionally, C2GnT1 mRNA levels are increased in colon carcinoma cells and may contribute to increased lymphatic invasion. The hypothesis being tested in the current set of experiments is that C2-O-sLeX forms high strength bonds with selectins, thus promoting adhesion and metastasis of cancer cells.

Over 100 tumor samples were examined for expression of C2-O-sLeX. Results revealed that colorectal adenocarcinomas and metastatic liver tumors express C2-O-sLeX, while normal colon and liver tissue and colorectal adenomas do not. Higher levels of C2-O-sLeX were seen in moderately and poorly differentiated tissue, while well-differentiated tissue exhibited lower levels of the glycoprotein. RT-PCR (reverse transcriptase polymerase chain reaction) showed that colon cancer cells have 15-fold higher levels of C2GnT1 than normal colon cells. Experiments in cell lines revealed that colon and liver cancer cell lines expressed high levels of C2GnT1 and FucT-III as well as high surface levels of C2-O-sLeX

The role of C2-O-sLeX in cancer cell binding to E-selectin, which is found on endothelial cells, was examined. Colon carcinoma cells that express C2-O-sLeX normally bind to E-selectin; however, when C2GnT1 expression was knocked down, resulting in reduced levels of C2-O-sLeX, binding to E-selectin was diminished. Lung and pancreatic cancer cell lines usually express very low levels of C2-O-sLeX; however, when these cell lines were transfected with the *FucT-III* gene, C2-O-sLeX on the surface of these cells increased, as did binding to E-selectin.

In summary, C2-O-sLeX is a tumor-associated antigen that seems to mediate binding of carcinoma cells to E-selectin. Future experiments will investigate the contribution of C2-O-sLeX to metastasis *in vivo*. The significance of C2-O-sLeX as a tumor marker and prognostic tool to predict patient survival will also be pursued.

Key Points of Discussion

- v The investigators are examining the function of cytoplasmic expression of C2-O-sLeX. They suspect that mucins may be present on the surface.
- v The investigators plan to do motility assays *in vitro* to determine whether C2-O-sLeX influences the motility of cancer cells, thus implicating it in metastasis.
- v The investigators are considering examination of the effect of C2-O-sLeX overexpression on E-cadherin.

- v Because so many steps are involved, it would likely be difficult to use protein levels of FucT-III and C2GnT1 as prognostic markers. It would be better to look at enzymatic activity.

The TRE17/Ubiquitin-Specific Protease 6 Oncogene Induces Inflammatory Cytokine Production Through Activation of NF-kappa B

Lashon Ussin, University of Pennsylvania

TRE17, also known as ubiquitin-specific protease 6, is an indirect effector of Cdc42 and Rac1, and is known to be involved in cortical actin remodeling and filopodial dynamics. It was initially identified as an oncogene as its overexpression in murine fibroblasts resulted in tumor formation in nude mice. Although TRE17 is absent from most adult human tissues except testes, it is highly expressed in tumors of mesenchymal origin.

TRE17 is thought to play a key role in the etiology of aneurismal bone cysts (ABCs). ABCs are pediatric tumors characterized by inflammatory infiltration and destruction of surrounding bone. These tumors contain multiple cell types, including osteoclasts, inflammatory cells, and stromal cells. TRE17 is highly expressed in 60 percent of these tumors due to translocation; however, its function in these tumors is unknown. Interestingly, nests of osteoclasts are often found near cells housing a TRE17 translocation.

The TRE17 protein has three major domains: the Rab GAP homology domain, a cysteine subdomain, and a histidine subdomain. The long form of TRE17 contains all three of these domains and induces secretion of inflammatory cytokines (e.g., IL-1 α , IL-1 β , MIP1 α), which play a role in osteoclast biology. In contrast, the short form of TRE17 is missing the histidine domain and is enzymatically inactive.

The mechanism by which the long form of TRE17 induces inflammatory cytokines is not well understood. However, experiments showed that treatment with an inhibitor of the transcription factor NF κ B blocked this effect. NF κ B is a rapid-response transcription factor that is involved in immune and inflammatory responses. It is activated in response to various inflammatory cytokines and viral infection. Under normal conditions, NF κ B is sequestered in the cytoplasm by its inhibitor I κ B. When I κ B is degraded, NF κ B translocates to the nucleus where it regulates transcription of target genes.

Experiments using an NF κ B-luciferase reporter construct revealed that the long form TRE17 (but not the short form) increases NF κ B promoter activity by more than 15-fold, suggesting that TRE17 causes increased expression of NF κ B. TRE17 also induced nuclear translocation of the p65/RelA subunit of NF κ B. To determine whether the effects of TRE17 on NF κ B are mediated through inflammatory cytokines, neutralizing antibodies were used to block α GM-CSF, MIP-1 α/β , IL-1 α/β ; these antibodies did not prevent NF κ B activation by TRE17, indicating that the inflammatory cytokines are not requisite mediators of this effect.

To gain insight into whether TRE17-mediated activation of NF κ B is through the canonical or noncanonical NF κ B pathway, a closer look was taken at the two IKK proteins. IKKs phosphorylates I κ B, causing it to release its hold on NF κ B and allowing NF κ B to move into the nucleus; thus, IKKs are, in essence, activators of NF κ B. Dominant negative forms of IKK α and IKK β were used to determine which of these proteins mediates the effect of TRE17 on NF κ B. Dominant negative IKK β but not dominant negative IKK α prevented induction of NF κ B by TRE17, indicating that the IKK β (which is part of the canonical pathway) is responsible for TRE17 activation of NF κ B.

In summary, TRE17 acts through NF κ B to induce production of inflammatory cytokines involved in osteoclastogenesis and osteoclast activation. This is the first molecular insight into how TRE17 could function in the pathophysiology of ABC and may lead to better understanding of TRE17's function in other bone neoplasms as well. Future directions include identifying TRE17's target in the NF κ B pathway, determining the signaling pathways involved in TRE17-induced NF κ B activation, and determining the effect of TRE17 on osteoclast biology.

Key Points of Discussion

- v The function of TRE17 in the testis is unclear. It is also expressed in mesenchymal stem cells.
- v TRE17 is only expressed in tumors. It influences the cell cycle through activation of ERK.

Translational Regulation of Myeloid Cell Differentiation: Novel Mechanisms and Players—PDCD4, DAP5, and IF2alpha

Bulent Ozpolat, UT M. D. Anderson Cancer Center-Houston

Approximately 33,440 new cases of leukemia will be diagnosed in the United States this year, and 21,700 individuals will die of the disease. The number of cases of leukemia has increased over the past 30 years. Among leukemias, AML is associated with the worst prognosis—only 20- to 30-percent survival rates are seen with standard treatment.

APL is a type of AML that is 3- to 6-fold more prevalent among Hispanic and Latin populations. APL is characterized by a translocation of chromosomes 15 and 17 that leads to expression of a PML-RAR α fusion receptor. ATRA, a derivative of vitamin A, is the standard therapy for APL. ATRA induces differentiation of leukemic cells and results in remission in up to 95 percent of patients.

The molecular mechanisms of ATRA-induced differentiation are not well understood. Gene expression profiling revealed that expression of approximately 3,000 genes is altered—1,300 are upregulated while 1,700 are downregulated. Furthermore, an 85-percent inhibition in protein expression is observed. Proteomics studies revealed that many proteins involved in translational control were downregulated after exposure to ATRA. Translational factors are overexpressed in many different types of cancer, and the resulting deregulation of translation may contribute to malignancy. Transfection of cells with many different translation factors leads to cell transformation. In normal cells, translation factors are regulated by cytokines, growth factors, and stress.

Based on these data, it was hypothesized that translational suppression plays a role in ATRA-induced differentiation of APL cells. Specifically, it was thought that ATRA suppresses translation by activating translational inhibitors (e.g., PDCD4, DAP5, p-eIF2 α) during differentiation. An APL cell line (NB4) and its maturation-resistant daughter cell line (NB4.R1) were used to test these theories.

PDCD4 inhibits translational initiation by blocking the activity of eIF4A; it is also a tumor suppressor and its expression is downregulated in many tumors. ATRA treatment of NB4 cells resulted in an upregulation of PDCD4 during granulocytic differentiation; however, PDCD4 was not upregulated by ATRA in the resistant NB4.R1 cell line. ATRA also induced PDCD4 expression in primary APL cells isolated from patients. To test the role of PDCD4 in ATRA-induced differentiation, PDCD4 levels were knocked down using siRNA. Cells with lowered levels of PDCD4 were unable to differentiate in response to ATRA.

DAP5 is also an inhibitor of translation. DAP5 levels increased in response to ATRA in APL and AML cells, but not in the ATRA-resistant NB4.R1 cells. Furthermore, downregulation of DAP5 using siRNA partially inhibited granulocytic differentiation of APL cells in response to ATRA. eIF2 α is another translational initiation factor. It is phosphorylated in response to ATRA in APL cells, and siRNA experiments revealed that it is necessary for ATRA-induced differentiation.

Together, these data indicate that ATRA acts on multiple levels to suppress translation of APL cells. Both cap-dependent and global translation are affected. ATRA activation of PDCD4, DAP5, 4E-BP1, and p-eIF2 α contributes to granulocytic differentiation. ATRA-resistant cells are unable to upregulate these translational inhibitors in response to ATRA, which may explain why these cells are unable to differentiate in response to ATRA. These data are consistent with the idea that lack of or altered translational control may be involved in disease pathogenesis and resistance/relapse in APL patients.

Future plans include determining the role of translational regulators in response to therapy, resistance/relapse, and survival in APL and AML patients; identifying downstream molecular targets of ATRA-induced differentiation in APL patient samples; and determining molecular mechanisms of ATRA resistance in APL patients using proteomics.

Key Points of Discussion

- v Although the effects of ATRA on translation are significant, they are not global. Translation of the mRNAs encoding housekeeping proteins is not downregulated as substantially as that of other transcripts.
- v ATRA can influence normal hematopoiesis—it affects expression of c-MYC and many proteins.

Concurrent Session I-2: Overview of Patient Navigation Programs

Moderator: Andrea Denicoff, Division of Cancer Treatment and Diagnosis, NCI

Development, Implementation, and Dissemination of a Patient Navigator Program With Hispanic Women From Community Clinics in South Texas

Kipling J. Gallion, The University of Texas Health Science Center at San Antonio

This project, implemented in South Texas, was a 2-year pilot to study the efficacy of a patient navigation program that uses a trained community lay health worker to help Hispanic cancer patients access cancer care services. The overall goal is to improve compliance and follow-up rates of Hispanics when they receive abnormal results from breast, cervical, and pelvic cancer screening tests. This should reduce lag time between screening and the treatment initiation. Additionally, the study aims to improve patient satisfaction with the healthcare system.

The study focused on Hispanic women over the age of 18 with abnormal cancer screening results. The participants were all patients at the Southwest or Southeast clinics of the University Family Health Center at The University of Texas Health Science Center in San Antonio. Participants were surveyed upon recruitment into the study and 6 months afterwards. Medical records provided clinical data about abnormal screening results. Out of 126 patients recruited, 41 were lost to follow-up (which peaked around 3 months), 82 completed the program, and 1 died due to a heart attack.

The most requested patient navigation services were liaison between patient and nurse practitioner, scheduling visits and reminder calls, financial aid, local resource identification, and translation of patient healthcare information. The study found it challenging to work with multiple Internal Review Boards and to obtain the correct credentials for accessing patient information and computer access to medical systems. Frequently, there were scheduling conflicts at clinics, and referrals were lost in busy obstetrics/gynecology clinics. Furthermore, there were a limited number of mammogram technicians at cancer therapy and research centers. Also, patients missed appointments and were unable to communicate with the clinics.

Next, the project will finish collecting data; continue to analyze data and disseminate results; and implement the project through *Redes En Acción*: The National Latino Cancer Research Network. The hope is to create a program that can be implemented in clinics using limited resources. A patient navigator training program was held in June 2008, and a training manual is being developed.

Overcoming Health Disparities Through Patient Navigation

Patricia Valverde, Denver Health/University of Colorado, Denver

Denver Health is one of nine sites throughout the United States that received one of the NCI Patient Navigator Research Program awards. Denver Health is the largest health care system serving the city of Denver. Its patient base is 52 percent Latino, 14 percent African American, and 27 percent white; more than 40 percent of Denver Health patients are uninsured. The project aims are to reduce the time from initial diagnostic screening to diagnostic resolution, reduce the time between cancer diagnosis and treatment initiation, increase adherence to standard of care guidelines, increase patient satisfaction, and perform cost analysis of patient navigation.

Patients are randomized to either the patient navigation intervention or a control arm (usual care without navigation). The study conducts baseline and postintervention surveys of patients, and major outcomes are submitted to a central data repository for a group-wide analysis. The program began with five patient navigators but currently has only three. Four of the original navigators were Latino and bilingual, and they included a master's level social worker, a counselor, and a physician. As of June 2008, 429 patients had been recruited (the overall goal for the 2-year project is to recruit 1,740 patients). The study faced challenges regarding enrollment, including patient consent, evolving standards of care, and the proliferation of patient navigation programs. The current patients include homeless and medically underserved patients, half of whom report having a first-degree relative who has had cancer. Nearly half of the participating patients are Latino, 19 percent are African American, and 24 percent are Spanish speakers. Approximately one-third of patients report having less than a high school education and only 22 percent work full-time. Half of the patients own a car and 55 percent own their homes. The study attributes recruitment success to specific recruiter characteristics: native Spanish speakers with extensive clinical trial recruitment experience. The recruiter meets patients during a medical appointment or through a home visit.

The navigators found it difficult to withhold help from patients in the control group, some of whom repeatedly called the recruiter. Other challenges included language barriers for patients who did not speak English or Spanish and limited resources that allowed a recruitment incentive of only \$10.

Patient Navigation Research Program (PNRP): The Washington, DC, Experience

Steven R. Patierno, George Washington Cancer Institute

Washington, DC, has one of the highest breast cancer mortality rates in the United States, and there is a significant disparity between blacks and whites. This may be due in part to late-stage diagnosis and delayed treatment initiation. Barriers to timely diagnosis include lack of a primary care physician, screening difficulties, lack of information, health insurance problems, poverty, and mistrust of the medical system. Washington's population is 58 percent black, 27 percent white, and 10 percent Hispanic. Each year, about 600 women are diagnosed with cancer and 120 die. Black women are twice as likely to die, though white women have higher cancer incidence. Additionally, cancer in black and Hispanic women presents at an earlier age and is generally more aggressive. Frequently, minorities will have clear symptoms of cancer and still not seek medical care. Washington has relatively reasonable screening rates but a very uneven distribution of resources, with one-quarter of the city's residents grossly underserved. Of 19 mammographic facilities, 13 are in Northwest DC, and only one is in Southeast.

The George Washington Mammography Van will visit the Anacostia area of DC twice a month for the next 3 years and will have a bilingual patient navigator available. The study intends to enroll at least 1,000 women with abnormal test results to investigate whether the use of patient navigation is more effective than usual care for decreasing the amount of time from suspicious findings to diagnostic resolution as well as the time between diagnostic resolution and treatment initiation. This study, which established the first citywide patient navigation program among nonaffiliated care centers, will collect data through 2010.

Overall, the patient enrollment rate is 35 percent, with a distribution that includes 58 percent black, 11 percent white, and 26 percent Hispanic.

Challenges to the program include cancer disparities on all levels, cultural psychosocial barriers, and citywide fragmentation of services. The original study design tested standard navigation versus enhanced navigation plus standard navigation. The program developed a network that included the George Washington Cancer Institute, Georgetown/MedStar, Howard University, Washington Hospital Center Preventorium, Washington Hospital Center Breast Center, Providence Hospital, Nueva Vida, and the DC Area Health Education Center. As patient navigation became more popular, several recruitment sites began offering enhanced navigation as their standard of care. Thus, the study was revised, consolidating the standard and enhanced navigation services into one arm and identifying a control group. However, this presents a challenge in that it is difficult to identify a control group that has not been exposed to patient navigation services. Thus, the program developed a concurrent records-based control arm with two data venues: women covered by DC government safety net insurance who did not get into one of the DC sites and records-based concurrent controls. Thus far, 170 patients and 160 control patients have been enrolled. Factors contributing to enrollment success included warm, accessible personalities of recruiters and clear physician support.

The Moffitt Cancer Center Patient Navigation Program

Kristen Wells, H. Lee Moffitt Cancer Center & Research Institute

The Moffitt Cancer Center Patient Navigation Program recruits patients from ten health care centers that provide care to medically underserved populations in the Tampa Bay area. The program utilizes four patient navigators and is targeting breast and colorectal cancer at all stages (from abnormal screening results to treatment). Clinic sites were randomized to patient navigator or control status. The times from abnormal screening to diagnosis and from diagnosis to treatment are measured by medical record abstraction. The population served by this project includes migrant farm workers, rural residents, and inner city residents in Florida. So far, the study has recruited 404 patients—80 controls and 324 who received patient navigation services. Demographic information was collected on race (63.8 percent white, 8.6 percent African American); ethnicity (71.6 percent Hispanic); gender (93 percent female); employment status (58.8 percent unemployed, 16.3 percent part-time employment); primary spoken language (66 percent Spanish); income (82 percent less than \$20,000); marital status (49.6 percent married); and education (mean years of education = 8.8). Of these patients, 313 had breast abnormalities, 85 had colorectal abnormalities, and 6 had both. To date, the problems of 57 percent of the patients have been resolved. A total of 11 participants have been diagnosed with cancer—one with colorectal cancer and the other ten with breast cancer.

The study faced several challenges, including the availability of affordable diagnostic colonoscopies. Additionally, patients had personal problems, such as drug and alcohol abuse, mental illness, physical abuse, other medical crises, and safety concerns. To address this, the group increased training for its patient navigators, paid attention to the identification and communication of potential safety threats, and conducted phone interviews with patients. Finally, the study had to deal with communication difficulties and lack of literacy among study participants. Thus, it utilized bilingual patient navigators, made all study and health education materials available in Spanish, used DVDs to provide educational materials, presented health information orally, and made interpretation services available to the patients. Next, the program will continue intervention testing, disseminate the group's findings and continue to work to address barriers to colorectal cancer diagnostic services.

Key Points of Discussion—Session I-2

- v PNRP is collecting data on number of interactions with patients and identifying barriers addressed during each encounter. Number of encounters/interactions will vary by patient need.

- v Principal investigators at Washington city-wide sites include African Americans and Latino/Latina. Almost all patient navigators and navigator supervisors are African American. The community advisory board is predominantly black.
- v PNRP navigators were surveyed to collect demographic information, education information, cancer survivorship, etc. Patient navigators have identification numbers that are linked to patient-related data. This will allow analysis to show which characteristics are associated with better patient outcomes.
- v The target patient population in DC seems unimpressed with technology. Models and posters are used for patient education. Technology is being used for training of patient navigators.
- v In Denver, a recruiter explains to prospective patients that the project needs a control group to determine whether patient navigation works. Participants in the control group receive cash incentives. The recruiter is a good sales person who is able to deal with doubts and concerns. She has extensive experience with clinical trial recruitment for Latinos; the program only needed to train her on the study protocol. A full-time recruiter became necessary because the program had low enrollment across all sites.

Concurrent Session I-3: Psychosocial Factors Associated With Cancer Disparities

Moderator: Maria Teresa Canto, Disparities Research Branch, CRCHD

Nalampasan Ko (I've Passed Through): Survivorship Among Filipinas With Breast Cancer

Nancy Burke, UCSF Helen Diller Family Comprehensive Cancer Center

This Community Networks Program, using the community-based participatory research approach, implemented a support system for Filipinas with breast cancer. One of its goals was to attract women most in need of breast cancer support resources by building on preexisting community partnerships and developing culturally appropriate outreach. This required identifying the specific cultural beliefs and values associated with breast cancer and survivorship and creating outreach themes based on these cultural values.

The United States Filipino population constitutes 18 percent of the overall Asian American population. A large portion (49.7 percent) live in California, and Filipinos make up 25 percent of the San Francisco Bay area Asian population. Oakland, California, also has a high percentage of Filipinos. Of the Filipinos living in California, 15 percent do not have health insurance and more than one in five are Limited English Proficient.

Initially, the cancer center partnered with the West Bay Pilipino Multi-Services Center *Sinag Tala* (Bright Star) Breast Cancer Support Group, but the partnership ended after four sessions. Subsequently, a second partnership was formed with the Pilipino Senior Resource Center. The 39 participants (4 male and 35 female) in the study ranged in age from 38 to 77 years old, had education levels ranging from elementary to college level, and had been in the United States between 1 and 50 years. Eighteen participants in breast cancer support groups were observed and detailed field notes were taken. Additionally, in-person qualitative interviews were conducted with support group facilitators and staff (n=6), women who had attended *Sinag Tala* (n=5), women who had never attended *Sinag Tala* (n=16), women who attended and stopped (n=3), and family members and caregivers (n=6). Additionally, two group interviews were conducted with two and six participants, respectively. Individual interviews were conducted in English, Tagalog, or a combination of the two, then transcribed verbatim and coded. Team members reviewed the transcripts, and discussed the content, codes, and themes of them in biweekly meetings. Coded data were

organized using Atlas.ti ethnographic software. Group interviews were conducted in Tagalog and analyzed in the same way as the individual interviews.

The study found that the Filipino population viewed cancer as simply another trial in life. To them, surviving cancer is not about self-preservation, but about family and the continued ability to help others. Additionally, being a cancer “survivor” means that one is entirely cancer-free. In conclusion, care must be taken with program names and labels, so that women who do not identify with the term “survivor” are not excluded from services. From a Filipino perspective, “survivorship” also calls up other challenges, such as immigration, discrimination, colonial history, violence, and familial expectations, which are also conceptually linked to “passing through” a trial in life.

The next steps for the study are to build on these findings to determine how breast cancer support services should be designed and delivered. Additionally, the group would like to disseminate its findings via the Filipino Community Press Club, community meetings, conferences, and peer-reviewed publications.

Social Support Needs of Samoan Breast Cancer Survivors

Sora Park Tanjasiri, California State University, Fullerton

Breast cancer accounts for 27 percent and 22 percent of cancer in female Samoan populations in Los Angeles County and Hawaii, respectively; however, there is only one Samoan-specific support group in the continental United States. In Orange County, California, native Pacific Islanders have the highest rates of mortality due to breast cancer compared to other ethnic groups.

Over the course of a year and a half, this study explored the social support needs of Samoan breast cancer survivors and their supporters (i.e., spouses, children, parents, siblings, or friends of survivor). Using social support theory as a framework, interviews and focus groups were conducted and the resulting qualitative data analyzed. Of the 24 originally targeted cancer survivors, 20 agreed to participate in the study, and 40 of the 45 supporters also agreed to participate. The majority of the cancer survivors included were over 50 years of age, had insurance or Medicare, and found their cancers in the early stages. The supporters were also usually 50 or older, married, and the parent or sibling of the cancer survivor.

Results showed that all of the cancer survivors faced loneliness, and 45 percent of them dealt with sexual intimacy issues as well. They also required logistical help from their supporters, and about 20 percent needed financial assistance. Nearly all of the survivors (90 percent) required assistance with decisions regarding diagnosis, treatment, or follow-up. Additionally, they wanted information on alternative medicine (60 percent), sexuality issues (40 percent), and the cancer process (20 percent). Eighty-five percent were church members and 65 percent utilized prayer.

Supporters of cancer survivors reported feeling sympathy for the survivor and being overwhelmed and fearful of recurrence. They also required emotional support for themselves, and many made the decision to get their own health checked.

In summary, the study recommends that cancer survivors share their experiences, promote cancer prevention, get emotional support, undergo sexual counseling, and provide support to others like themselves. Supporters need to help promote early detection and prevention, show support for others, and focus on a healthy lifestyle for themselves. The next steps for this CBPR project include continued data analysis, implementation of a church-based patient navigation program, continued academic dissemination of this information, and working with decision makers for ongoing support to their communities.

The Relationship Between Self-Identity and Depression in Women From Appalachia, Ohio

Douglas Post, Ohio State University Department of Family Medicine

This research aimed to explore the link between Appalachian self-identity and symptoms of depression in women. Depression is a common and often debilitating condition that affects about 6.6 percent of the United States population for at least 12 months and about 16.2 percent for their entire lifetimes. With a high prevalence in rural areas, it is the leading cause of disability in the world and the fourth-leading contributor to disease. A sample taken from a rural clinic that included people with Type 2 Diabetes from Appalachian Ohio and West Virginia showed a 31-percent rate of moderate to severe depression. Other correlates for depression include being female, young, divorced or widowed, low-income, uneducated, and unemployed.

Appalachia consists of both rural and urban areas in 410 counties and 13 states across the East. The area, which is divided into northern, southern, and central regions, has a high rate of unemployment, poverty, disability, and low education levels. The Appalachian region of Ohio is primarily rural and shares a similar historical background with eastern Kentucky and West Virginia; thus it was designated an official part of Appalachia by Congress in 1965.

Common stereotypes, migration patterns, and diversity cause some people not to self-identify as “Appalachian.” A recent study showed that women who self-identified as “Appalachian” had lived in a rural area for a long time, had family ties to the region, and were religious. Furthermore, a strong ethnic identity has been shown to cause emotional and mental distress, especially when an individual has experienced prejudice and marginalization.

The study obtained a list of patients from area Community Awareness Resources Education clinics and selected monthly random samples of women who had been seen at the clinic within the last 2 years; were at least 18 years old; had no history of cervical cancer or hysterectomy; and lived in the rural areas of Appalachian Ohio. These women were contacted with an initial survey (mailed or given to them by a research interviewer) and a follow-up phone call. Additionally, researchers conducted face-to-face interviews that lasted about an hour and a half each. The questionnaires included inquiries into whether the women identified themselves as “Appalachian” and used the Center for Epidemiologic Studies Depression Scale (CES-D) to assess mental health; a score of 16 or more indicated depression.

The study found that women who tested positive for depression were more likely to be young, unemployed, less educated, poor, married, isolated, and smokers. Of those women who tested positive for depression, 28 percent identified themselves as “Appalachian,” and 38.3 percent of the women surveyed who were not depressed also identified themselves as “Appalachian.” Thus, the odds of depression actually decreased with self-identification as “Appalachian.”

In summary, women who reside in Appalachia, Ohio, have a high prevalence of depression, which correlates with many facts that have been identified by previous research. For the most part, self-identification as Appalachian has a protective effect on women when it comes to depression. This may be due to regional stability and strong religious affiliations. The only area studied that did not show this protective effect was a rural area that was in close proximity to an urban area and had an older population, fewer economic resources, and fewer close contacts. The study was limited by the fact that it utilized the CES-D, which is not a diagnostic tool for depression. Additionally, the limited sample of participants may not represent the entire population; self-reporting mechanisms may be unreliable; and measurement of self-identity is difficult. However, this is the first study that has been undertaken to assess the role of Appalachian self-identity in depression; it indicates that reinforcing Appalachian self-identity may provide a protective effect against depression.

Challenges to Conducting Community-Based Genetics Research in Puerto Rican Communities in the United States and in Puerto Rico

Gwendolyn Quinn, H. Lee Moffitt Cancer Center and Research Institute

This study assessed challenges researchers face in CBPR studies focused on genetics. There is increased incidence of ovarian and breast cancer in carriers of the BRCA1 gene mutation. Other genes that increase the risk of cancer include BRCA2, TP53, LKBI, PTEN, and HNPC, though researchers have not yet identified all of the genes associated with this disease. People with a risk of hereditary breast cancer are advised to begin mammography at an earlier age than those who do not have that risk. Other treatments that are contemplated are risk-reducing mastectomy, salpingo oophorectomy, and drugs such as tamoxifen, raloxifene, and oral contraceptives. Rates of testing for BRCA1 and BRCA2 mutations are not equal among different ethnic groups. Analysis of a database of 10,000 BRCA-tested women revealed that 41 percent were of western European ancestry, while only 2.3 percent were Latin American, 2.2 percent Native American, 1.6 percent African American, 1.1 percent Asian, and 0.9 percent Middle Eastern.

This disparity is caused in part by a lack of awareness and knowledge of cancer. A lack of access to genetic services, coupled with cultural barriers, is also a factor. This study was designed to examine at-risk Hispanic women's knowledge, attitudes, and intentions regarding genetic counseling and testing. The study included women between the ages of 18 to 65 who had a personal history of breast or ovarian cancer. Also included were women over age 50 who had a mother or sister with breast or ovarian cancer and women of any age who had any female relative with a history of these types of cancer. The participants in the study self-reported their ethnicity as Puerto Rican, Cuban, or Mexican. The goal, after assessing the population's attitudes and behaviors regarding genetic counseling, was to develop a culturally relevant campaign that would decrease the disparity in testing for mutations. The researchers conducted face-to-face interviews that lasted 60 to 90 minutes. The interview guide they used was developed based on previous literature and input from an expert panel. It included a questionnaire and quantitative instruments. Originally, the study sought to include 60 women from local clinics, but found that women were very busy; many of them had small children. These women were also concerned about other health issues. Recruitment flyers promising compensation were mainly distributed at local businesses, but were also present at health fairs, at the Department of Health, and in newspapers. In the end, the study included only 32 participants, recruited mainly with the help of locally-placed flyers. Other problems the study faced with regard to recruitment were lack of knowledge about specific types of cancer, availability for only telephone screening, low numbers of Cuban and Mexican participants, and the fact that some interested in the study had already had genetic testing done.

In summary, the study found some valuable information about the materials used. Participants do not always find medical translation to be meaningful. Brief materials were most effective. The review panel turned out to be a valuable part of the development of the study. The most effective methods for recruitment were flyers and press releases, as well as approaching women at a time when they were not concerned with other matters. Additionally, the study found that it was sometimes difficult to obtain information about family health history.

Concurrent Session I-4: Communicating Effectively With Policymakers

Moderator: Jeanette Contreras, Office of Government and Congressional Relations, NCI

Power of Advocates for Patient Care

Robin Squellati, Office of Senator Daniel K. Inouye

Last year, the overall NIH budget was increased by approximately \$1 billion; however, not all programs received additional funds. Lobbying policymakers is one way to try to secure funds for a program; indeed,

Senators' offices receive many visitors who are lobbying for a variety of things, including increased funds for cancer research. Advocates should keep several issues in mind as they communicate with Congressional offices. Congressional staffers may not be knowledgeable about the healthcare field, so the use of acronyms and abbreviations without explanation is not advisable. Also, many Senate offices are relatively small and cannot accommodate large groups of people. To make optimal use of the limited time of Congressional members and their staff (most meetings are only 20 to 30 minutes long), issues should be concisely presented in a one-page summary. If a Senator asks how he/she can help advance an issue, advocates should be prepared to provide a few concrete suggestions (asking for too much will likely be counterproductive). Finally, advocates need to be familiar with the political process. For example, it is important to understand that the Senate and House of Representatives usually develop and pass different bills. Advocates should also know which Congressional members support a particular issue or bill.

Navigating Relevant House Congressional Committees

Julie Rones, Office of Congressman Edolphus Towns

Advocates should become familiar with Congressional committees and subcommittees and understand the jurisdiction of committees that may be relevant to a particular issue. In addition to passing legislation, many committees also perform oversight of federally funded programs and agencies. It is important to get to know committee members and their personal staff as well as committee staff. Advocates also need to recognize that each committee operates under different rules; it is advisable to develop an understanding of the rules governing committees of interest.

Advocates also need to be knowledgeable about the political process and the role of Congressional hearings. Proposed legislation may be introduced simultaneously in both the House and Senate, or it may be introduced in one chamber before the other. When legislation is introduced, it is referred to the appropriate committees or subcommittees for review and action. Each committee considers member requests for hearings and establishes a hearing schedule. The committee often holds hearings with witnesses before a proposed bill undergoes markup (the process by which committees and subcommittees debate, amend, and rewrite proposed legislation) at the subcommittee and/or committee level. Revised legislation must usually be passed by the full committee before being sent to the whole House or Senate for a vote.

Timing can be very important when trying to pass legislation. Advocates must know when their target committee will be addressing certain issues. For example, the President releases his budget proposal to Congress in February; the House Budget Committee often holds hearings on the proposal in March, providing opportunity for members, caucuses, and the public to express concerns and/or offer alternative proposals. Advocates should consider when it would be most beneficial to ask a member to introduce legislation, propose an amendment, co-sponsor a bill, deliver a speech, sponsor a briefing, establish a Congressional caucus, or promote a Congressional hearing. Advocates must also understand that it may take several attempts to pass a bill—of the approximately 10,000 measures introduced in Congress in a given year, only an average of 400 will pass.

Many factors influence the passage of a bill. Committee chairs may limit the number of pieces of legislation committee members can put forth. Thus, committee members are often required to prioritize their interests; advocates must think strategically about which members will be most likely to consider their issue a high priority. It may also be helpful to call and e-mail members to educate them and let them know how passionately the public feels about a measure. Budget issues can also influence the passage of a bill. The current Congress requires that implementation costs associated with a bill be accounted for prior to its passage; thus potential legislation is reviewed and scored by the Congressional Budget Office. A poor score may discourage members from advocating strongly for a bill. Committee chairs have considerable power over the legislative process; they may prevent rank-and-file committee members from directly taking part in negotiations regarding a bill. In this case, members or groups of members must

communicate with the Chair or others in leadership to emphasize important issues. Members may also need to work together to promote the need for hearings and markup sessions. Members sometimes try to build support for their interests by distributing “Dear Colleague” letters to other members. Committee chairs and others sometimes use “consensus strategy” to enable passage of controversial bills. This generally involves extensive behind-the-scenes negotiations to build support from both parties. In general, interpersonal dynamics between members can have a strong influence on the advancement of legislation; advocates should take these dynamics into account when developing lobbying strategies.

Congressional District Interactions

Joan Kleinman, Office of Congressman Chris Van Hollen

District offices are located within the home district of each Congressional member. Because they are located within the community, these offices interact directly with members’ constituents and often hear suggestions and complaints before they reach Capitol Hill. District office staff members often act as “problem solvers” for constituents, answering questions and obtaining information to address concerns. Advocates should strive to be a resource for district office staff; it is important to educate staff about issues and let them know how they or the Congressional member can better serve the community. Advocates who want to meet with someone at a district office should call or e-mail to set up an appointment. Inviting the Congressional member to community events is also encouraged; if the member cannot attend, he/she will likely send a representative.

Working as the TriCaucus to Reduce Health Disparities

Noelle Lee, Office of Congresswoman Hilda Solis

There are 10 staff members in the office of each House of Representatives member, compared with 30 staff members in each Senator’s office. Thus, each House staff member must handle multiple issues simultaneously; advocates must be mindful that staff will not be expert in all areas. Additionally, advocates must be aware that there are several committees with jurisdiction over health issues and each has different responsibilities. For example, authorization committees set up new programs, while appropriations committees approve funding for programs.

When communicating with a Congressional office, it is important to clearly explain the importance of a particular issue and provide information in lay terms. Advocates can also make suggestions for ways members could advance a particular cause.

Things to Remember—Reflections From an Advocate

Grace L. Butler, Hope Through Grace, Inc.

Although advocates feel passionately about a particular issue, it is important to remember that each Congressional member must tend to multiple issues. When communicating with members, it is important to explain how a particular interest relates to issues important to them. Advocates should have a strategy for communication, which may include developing one-page summaries, making phone calls, and sending e-mails. Because members have limited time, it is important to be concise as well as accurate. Members will be most responsive to their constituents’ identified interests, so it may be beneficial to garner support in the community before approaching legislators. Congressional staffers are an important part of the process; it is important to develop relationships with them and acknowledge the support they provide.

NCI’s State Cancer Legislative Database: A Resource for Policy Analysis

Kerri McGowan Lowrey, The MayaTech Corporation

The State Cancer Legislative Database (SCLD), which can be accessed at <http://www.sclld-nci.net>, is a collection of bill summaries and enacted state statutes. “Disparities” was added to the database as a new

topic area in September 2007. The current study used SCLD to examine the extent to which states have passed laws addressing cancer disparities and determine the types of legislation that have been enacted. To do this, searches were carried out to identify legislation with term “cancer,” its synonyms, or language most likely meant to include cancer (e.g., life-threatening disease) in the same paragraph as a selected population term (e.g., Hispanic) or terms like “health disparities” or “health inequities.”

The search revealed that “health disparities” is a broad topic and can refer to different racial ethnic populations, socioeconomic groups, and other populations (e.g., age groups, immigrants, urban/rural). The database monitors activities related to: (1) acknowledgment of a problem (i.e., the legislature has acknowledged a problem but has not yet addressed it); (2) primary prevention (behavioral and environmental risk factors); (3) research; (4) screening and treatment information; (5) screening and treatment programs; (6) state capacity; and (7) workforce diversification and training.

This research has demonstrated the need for policy action to address the symptoms and social and systemic causes of cancer disparities. The District of Columbia and all 50 states have addressed the problem by enacting laws regarding access to primary prevention and treatment, workforce diversity and training, research, and public awareness. One limitation of this database is that it does not include state administrative regulations, Attorney General opinions, executive orders, court decisions, or local ordinances. Other factors such as education, environmental justice, and fair housing laws are not included in the database but can also have a profound impact on health disparities, and any comprehensive effort to address the roots of inequalities should include them.

Key Points of Discussion—Session I-4

- v Congressman Towns is sponsoring several bills on prostate cancer and one to establish an office of men’s health to give men the attention that is desperately needed.
- v The best way for a scientist to make the transition to policy-related work on Capitol Hill is to obtain a fellowship. Many Congressional caucuses (e.g., Congressional Black Caucus) provide fellowship opportunities, as do some individual Congressional members.
- v The Patient Advocacy Foundation is a good source of information on how well third-party insurers are doing in providing reimbursement for treatment provided in clinical trials. The SCLD is also a source of information on this subject.
- v The most important way advocates can ensure that their message is heard and understood by legislators is to develop clear, concise written materials.
- v Legislation to regulate the tobacco industry is finally being considered. One bill aimed at preventing tobacco use by children contains language that would eliminate flavors from cigarettes.
- v One important way to increase minority participation in clinical trials is to develop public education programs aimed at reducing fear of clinical research. People need to know that their health will not be harmed and their identities will be protected.

Concurrent Session I-5: Colorectal Cancer: What Approaches Work in Reducing Disparities?

Moderator: Vickie Shavers, Division of Cancer Control and Population Sciences (DCCPS), NCI

Colorectal Cancer in Minority Populations

Vickie Shavers, DCCPS, NCI

In 2008, 11 percent of new colorectal cancer diagnoses and 14.1 percent of colorectal cancer-related deaths occurred among African Americans. There has been a significant decrease in deaths caused by

colorectal cancer among whites since 1970, but this trend has not been seen in minority populations. New guidelines for colorectal screening suggest that prevention, not early detection, is the best way to deal with colorectal cancer.

There are two screening methods for colorectal cancer: flexible sigmoidoscopy and colonoscopy. Flexible sigmoidoscopy is very accurate for detecting cancer in the first third of the colon. Generally, it is combined with a blood test, called the Fecal Occult Blood Test, which detects trace amounts of blood in the stool and can detect cancer forming in all parts of the colon. Colonoscopies examine the entire colon and are most commonly used to detect most colorectal cancers. However, since only specialists may perform colonoscopies, health maintenance organizations and other third-party insurers may not cover this service. Additionally, the discomfort and embarrassment associated with colonoscopies may prevent some people from being screened. Colonoscopies are more accurate, time-consuming, and expensive than the alternative, though any screening is better than none at all. Thus, the focus should be on getting people access to screening for colorectal cancer, regardless of the method.

Addressing Colorectal Cancer Disparities in Arkansas

Paul Greene, University of Arkansas for Medical Sciences (UAMS) College of Public Health

The Arkansas Colorectal Cancer Act mandated insurance coverage for colorectal cancer screening, defined screening and reimbursement guidelines, and established a control program to assess needs and capacity for screening. Dr. Greene and his colleagues conducted a phone survey of 2,021 random people to determine screening histories and factors associated with the decision to be screened. The sampling procedure stratified the population of Arkansas so that the study could examine regional differences within the state. Additionally, the study over-sampled to ensure that minority populations were represented.

The survey showed that the highest percentage of screening occurred within the central part of the state and that the southeast region had the lowest rate of screening. The percentages of people who had been screened also correlated with the number of primary care physicians and specialists in the region. Additionally, the study found that primary care visits factored importantly into whether people received screening. Sociodemographic factors may also contribute to screening differences among regions.

Future efforts aimed at increasing colorectal cancer screening should foster engagement between primary care providers and community members; cultivate collaborative efforts between physicians and endoscopy facilities; promote all screening methods; and facilitate access to Medicare and Medicaid. It is important for a public health initiative to minimize out-of-pocket expenses; accommodate people with lower income and education levels; and employ staff who are aware of cultural difficulties regarding screening. Navigators who can help patients identify and deal with obstacles to screening and treatment are also essential, as are community role models who can help promote positive attitudes toward screening.

A Community-Centered Approach to Developing and Pilot-Testing a Colorectal Cancer Education Campaign for Pacific Islanders in California

Alek Sripipatana, California State University, Fullerton

The CNP campaign this team developed is called Weaving Islander Network Cancer Knowledge, Attitude, Beliefs, and Behaviors (WINCKABB). The goals were to recommend methods of educating the public on colorectal cancer; design and pre-test campaign materials; and ensure that the campaign was culturally appropriate and effective. Educational materials employed by WINCKABB included a flipchart, bookmark, and public service announcement. The campaign's primary messages were "Ask your doctor about colorectal cancer screening" and "Do it for yourself and your family." The campaign was culturally tailored by employing a variety of techniques, including constituent involvement and

evidentiary statements; use of peripheral images; paying attention to sociocultural cues (for example, the emphasis on family values); and in-language translations of the materials. Constituent involvement was especially important to the team, since the campaign is based on CBPR and thus places an equal emphasis on both academic and community participation. In pre-testing materials, special attention was paid to the appropriateness of language and pictures, content on colorectal cancer, and font size. For testing, 38 participants (both male and female) were divided into 5 focus groups. Participants ranged widely in age, education level, and Asian descent.

Feedback from the community indicated that the brochures should be more culturally specific (e.g., brochures passed out to Samoans should feature pictures of Samoan people), a diagram of the colon should be placed on the front of the flipchart, and text in the materials should be more concise. The plan for pre-implementation of the campaign includes testing revised versions of the materials, a pre-test evaluation plan, and a study design/evaluation plan.

Screening Colonoscopy Completion Rates Among Patients of African-American Primary Care Physicians Trained in Colonoscopy

Sudha Xirasagar, University of South Carolina

Screening colonoscopy is the best method for preventing colorectal cancer; 90 percent of colorectal cancers and deaths from colorectal cancers are prevented this way. However, there are not enough specialists and only about half the population is currently being served. African Americans are more likely to suffer from colorectal cancer, but they are less likely to receive a colonoscopy. The goal of this study is to determine whether more training for primary care physicians can reduce this disparity. To do this, the quality and safety of colonoscopies performed by primary care physicians were assessed, as was the impact of these factors on African-American patients' compliance.

In the midlands region of South Carolina, experts trained primary care physicians in colonoscopy and supervised them for up to 50 procedures. After this training, physicians were given access to an endoscopy center with an expert on staff to assist, if necessary. If a patient preferred an expert, the primary care physician referred them to one; otherwise, the physicians were instructed to bring their patients to the endoscopy centers. The study reviewed data on 200 patients who were seeing one of six African-American physicians trained in colonoscopy procedures. Additionally, it analyzed data generated by six untrained African-American physicians and compared patient compliance rates between the trained and untrained physicians' patients. Currently, the data compilation is nearly complete, with only one trained physician's and one untrained physician's data pending.

Preliminary statistics show that about 75 percent of the patients included are African American, 20 percent white, and 5 percent of another ethnicity. Additionally, 65 percent were female and 35 percent were male. The majority of the patients were between 50 and 64 years old, and all had private insurance or Medicare/Medicaid. Untrained physicians treated more African Americans, more females, and more patients with private insurance than trained physicians; there were no significant differences between physicians in the ages of patients treated.

Concurrent Session I-6: Models of Training Programs: Advancing Diversity

Moderator: Dorkina Myrick, Cancer Training Branch, NCI

Research Opportunities in Medical Physics for Graduate Students of Hispanic Origin: The UTHSCSA Experience

Alonso Gutiérrez, The University of Texas Health Science Center at San Antonio

The Medical Physics Program was established within the University of Texas Health Science Center San Antonio (UTHSCSA) School of Medicine in 1989. The program offers Ph.D.s in Radiological Sciences with specialization in Radiation Therapy, Diagnostic Physics, Radiation Biology, Human Imaging, and Neuroscience Imaging. Currently, the program has 30 faculty members and 60 Ph.D. students. One part of the training mission of the program is to reduce cancer health disparities in radiation oncology by increasing the number of Hispanic medical physicists. Hispanic medical physicists can help address disparities by improving cancer treatment awareness within the Hispanic community, minimizing the cultural barriers between Hispanic cancer patients and health care professionals, and researching novel methods of improving the efficacy of radiotherapy for cancer patients. The program has already graduated four Hispanic students, three of whom were women. There are currently four additional Hispanic students enrolled in the program.

Efforts are made to recruit Hispanic undergraduate and Masters-level students majoring in physics at a number of in-state universities, including branches of the University of Texas at El Paso (UTEP), San Antonio, Pan American, and Brownsville. Collaboration with UTEP through the MI/CCP P20 partnership allows Hispanics working toward their Master's in Physics at UTEP to initiate a Ph.D. research project during the second year of the Master's program and then transfer to UTHSCSA to complete their Ph.D. studies.

Hispanic Ph.D. students in the UTHSCSA program participate in a number of research studies. These include characterization of the dose calculation accuracy of current treatment planning systems in the treatment of lung cancer; development of novel metrics for patient-specific 3D/4D dose delivery quality assurance; and quantification of contralateral breast dose during whole breast irradiation (to reduce the chance of secondary malignancy).

Future plans of the program include seeking funds for the continued training of Hispanic students in medical physics; the goal is to recruit a minimum of two Hispanic students per class. Efforts will also be made to strengthen the research collaboration with UTEP and to aid UTEP in the development of a Master of Science program in medical physics. The program also hopes to establish recruitment ties with other universities.

Key Points of Discussion

- v Because students receive a great deal of attention from faculty and are highly motivated, retention rates of the UTHSCSA program are high.
- v Other institutions have expressed interest in replicating this program, but manpower remains the primary barrier to expansion.
- v After graduating from the program, most students remain in academia and focus on health disparities research. A few have entered private facilities but continue as adjunct faculty.

Increasing Minority Representation in Radiation Oncology Physics

Marian Manciu, University of Texas at El Paso

There is a shortage of medical physicists in the United States and a shortage overall of Hispanics in cancer research. It is thought that increasing the number of Hispanics in radiation oncology may help improve cancer care for Hispanic patients. The main objective of the current program is to increase minority representation in radiation oncology physics through a dual degree program that allows students to earn an M.S. in physics from UTEP and then a Ph.D. in Medical Physics from UTHSCSA. The collaboration has resulted in new classes in medical physics being offered at UTEP and the offering of distance learning classes through UTHSCSA.

UTEP has expertise in computational, theoretical, and solid-state physics. UTEP researchers have participated in a number of collaborative research projects with UTHSCSA researchers. Some examples include projects entitled “X-ray Spectral Estimation from Attenuation Measurements” and “Modulation Transfer Function above Nyquist Frequency.” The program also has a community involvement component. Local medical physicists interface with the program and partnerships are in place with local cancer centers and hospitals. Outreach is also conducted at local high schools and community colleges.

Since the inception of the program, which is funded through an MI/CCP P20 grant, four underrepresented minority students have been recruited into the program. Also, four M.S. students have been accepted to the UTHSCSA Ph.D. program. In the fall of 2008, UTEP will be implementing a B.S. in Physics with a concentration in Medical Physics; these students will have a major in Physics and minors in Mathematics and Biology. A Master of Science program in Medical Physics is also being planned and will likely begin in the fall of 2009.

Key Points of Discussion

- v An introduction to medical physics is an elective for undergraduates and is required for masters students.
- v Masters students often initiate a research project in their second year at UTEP in collaboration with UTHSCSA. This research can be continued into the Ph.D. program at UTHSCSA.
- v Some students may be lost to this field due to the opportunity of applying to enter medical school. However, most prefer to remain involved in the physical sciences. A few choose to become involved in radiation-related medical specialties.

Designing and Implementing Successful Research Training Programs for Native American Students in Arizona

Louise Canfield, University of Arizona

Less than one percent of cancer researchers and less than one percent of oncologists in the United States are Native American. The goal of the Native American Cancer Research Partnership (NACRP) is to increase the numbers of Native American researchers and oncology-related healthcare professionals in Arizona and the Southwest. There are challenges related to recruitment, training, and retention. There is a relatively small pool of students from which to recruit and many Native Americans distrust research and researchers. There are also few existing research-centered programs to which to recruit students, and it can be difficult to get relevant courses inserted into already crowded curricula. Retaining Native American students can be difficult because these students often have to deal with limited financial resources, as well as family expectations and responsibilities.

To address some of the challenges with recruitment, NACRP is creating partnerships with universities and the community and engaging in publicity/marketing. Key university partners include the University of Arizona (UA) Cancer Center and Northern Arizona University (NAU). Community partners include

Dine' College, Tohono O'odham Community College, Pima Community College, Coconino Community College, the Community Advisory Board, and the Program Steering Committee. For publicity and marketing, NACRP has developed a Web site, brochures, and newsletters.

Solutions for challenges related to training include enlisting community partners, gaining institutional support, and leveraging resources. Support has been obtained through a number of UA and NAU offices and departments. For UA, these include the Cancer Health Disparities Institute, Multicultural Affairs, American Indian Studies, Department of Chemistry, and Career Services; these entities share funding in the form of a P30 supplement, minority supplements, and an R25 training grant. At NAU, the Chemistry/Biochemistry department, Applied Indigenous Studies program, and other groups support NACRP; these groups share an area R15 grant.

UA has an undergraduate program that includes classes specifically tailored for Native American freshman; these courses inform students about careers in oncology for Native Americans and discuss the interface between western science and native knowledge. Chemistry labs for Native American students are offered to sophomore chemistry students. Junior and senior students are encouraged to do laboratory research. Students of all ages take place in summer research, the Pathfinder program, and national programs. Undergraduates can also participate in research rotations at the Arizona Cancer Center. This program, which is part of the CURE program, involves a 6-week orientation to laboratory research, three 6-week rotations in laboratories, and then assignment to a cancer center laboratory. The Arizona Cancer Center also has an NCI R25 postdoctoral training grant, which funds recipients for 2 years; to date, six recipients have been selected (one Native American and one Hispanic).

The NAU curriculum includes an M.S. in Chemistry with an emphasis in Carcinogenesis and Cancer Chemotherapy as well as an Indigenous Health Studies minor and the opportunity for independent research.

The Pathfinder program was developed by students in response to the community's need for cancer treatment education. Students undergo a 40-hour intensive summer training program, which includes an introduction to cancer biology and disparities as well as issues related to cancer screening, diagnosis, and treatment. The students then spend 4 weeks in a Native American-serving healthcare facility working with community outreach and education staff.

NACRP has identified a number of approaches to improve retention and graduation rates. These include establishing core values, identifying strong mentors, providing culturally competent training for mentors and teaching faculty, and developing strong community relationships. NACRP's core values include support, commitment, communication, and respect. Mentors for NACRP students are selected very carefully and are formally trained; those with experience mentoring underserved students are used as often as possible, as are Native American mentors. Efforts are also made to facilitate the creation of communities by encouraging Native American students to interact with one another. Mentor training includes IRB training for research in Native Nations, cultural competency workshops, and the Indigenous Summer Seminar Series at NAU.

Between 2002 and 2008, 116 Native American students were trained through NACRP programs. Of these, 54 were involved in long-term research projects/programs, 15 conducted summer research, 47 received didactic training, and 1 received a postdoctoral fellowship. Thirty-nine Native American students have received degrees (27 Bachelors, 11 Masters, 1 Ph.D.). Several former NACRP students are currently employed in health care professions (4 public health professionals, 2 nurses, 5 research technicians). Several former students are also pursuing professional and graduate degrees.

Several lessons have been learned through the NACRP experience. It is important to:

- v Develop and maintain core values.
- v Create an identity (Web sites, logos, brochures, videos, newsletters).

- ✓ Set realistic goals for recruitment and retention.
- ✓ Establish university and community partners.
- ✓ Develop courses that can be integrated into institutional curricula.
- ✓ Institute stronger articulation programs between tribal/community colleges and universities.
- ✓ Create communities among students and mentors.
- ✓ Provide strong mentors and monitor the process.

Future directions of NACRP include fortifying the pipeline by strengthening ties with community/tribal colleges, developing stronger articulation programs, enhancing internship programs, and expanding efforts to high school and middle school students.

Key Points of Discussion

- ✓ Trainees are dedicated to providing services to their own communities. Unfortunately, research opportunities in Native American communities are rare.

Diné College/Mayo Clinic: Development of Cancer Education and Research Training Programs for Navajo Students

Christi Patten, Mayo Clinic

An NCI P20 planning grant was awarded to the Mayo Clinic and Diné College (a minority-serving institution) to develop a program for cancer education and research training for Navajo students. The purpose of the program is to increase the number of Native American students pursuing advanced degrees in the public health and biomedical fields by providing opportunities to obtain experience in cancer research and training. This may ultimately help reduce cancer risk behaviors and decrease the mortality rate among Native Americans (currently the second leading cause of death).

One of the aims of the P20 grant is to develop a student curriculum for cancer education. One component of this is the Summer Research Enhancement Program (SREP), a 10-week research training program in public health research methods for Native American undergraduate students at Diné College. It includes both didactic and experiential learning elements. The course was developed through face-to-face meetings of Diné College and Mayo Clinic faculty with input from an Advisory Committee and a community advisory group. SREP focused on diabetes research for the first 7 years, but added cancer as a focus in 2007. Pre- and post-program assessments showed that the students became more knowledgeable and felt they were more capable of carrying out research. All 11 of the students who participated in the 2007 program said they would recommend it to another student.

Another component of the P20 grant involved developing a cancer research experience for Diné College students at the Mayo Clinic. The program, called Native CREST (Cancer Research Experience and Student Training), drew on SREP as well as SURF (Summer Undergraduate Research Fellowship), a Mayo Graduate School program. As part of the development process, the level of integration with SURF was determined, the program name and logo were generated, recruitment and application materials were designed, and a long-term tracking system was created. An e-mail survey of Mayo investigators identified 33 potential mentors for the program. In preparation for the program, a presentation was given to the researchers on how to mentor Navajo students in research. The program was piloted in the summer of 2008; two students selected from a pool of six applicants participated.

Next steps include revising the cancer SREP program based on feedback from 2008 participants and developing a cancer-focused course at Diné College. The Native CREST program will also be revised based on feedback from the 2008 pilot program and another pilot will be conducted in 2009 at both the Rochester and Scottsdale campuses.

Key Points of Discussion

- ✓ Some of the summer courses have been incorporated into the Diné College catalog. This is the only native school with a public health degree program.

National Training for Patient Navigators

Elizabeth Calhoun, University of Illinois at Chicago

The national training for patient navigators working at the nine PNRP sites is designed to ensure that all navigators are provided with core competencies in several domains, including client interaction, care management, intervention delivery, and documentation. The curriculum is intended to standardize training throughout the project so that investigators are able to control for training effects as they evaluate the effectiveness of patient navigation.

Topics covered in the national PNRP training curriculum include:

- ✓ Basic information about cancer.
- ✓ Overview of health disparities.
- ✓ Introduction to clinical research.
- ✓ Roles and responsibilities of patient navigators.
- ✓ Communication skills.
- ✓ Culture and diversity.
- ✓ Resource mapping.
- ✓ End-of-life issues.
- ✓ Financial aspects of health care.

Evaluation of trainees focuses on skills rather than theoretical knowledge. Communication and care management skills are measured using “objective structured clinical examination” methods, including role-playing.

Key Points of Discussion

- ✓ As core competencies become more clearly defined and training methods to instill them are refined and formalized, patient navigation has the potential of developing into a new health care profession.
- ✓ PNRP training emphasizes the difference between appropriate navigator activities, such as delivering prepackaged information, and inappropriate activities, such as delivering test results to patients or describing possible side-effects of treatment. Knowing when to ask for professional assistance is a key skill for navigators.

Concurrent Session II-1: Molecular Mechanisms and Cellular Targets

Moderator: Peter Ogunbiyi, Diversity Training Branch, CRCHD

Uncovering the Mechanism of Cell Death Induced by Saporin Delivered Into Cancer Cells by an Antibody Fusion Protein Targeting the Transferrin Receptor

Tracy Daniels, University of California, Los Angeles

Transferrin receptor (TfR) mediates iron transport across the plasma membrane via receptor mediated endocytosis of iron bound to transferrin. TfR is an attractive target for cancer therapy because it is

elevated on cancer cells and internalized when bound by ligand. The anti-hTfR antibody IgG3-Av is one example of a potential therapy that targets TfR. This antibody exhibits intrinsic cytotoxic activity against malignant hematopoietic cell lines. It also alters the trafficking of TfR, leading to downregulation of surface TfR and eventually leading to lethal “iron starvation.”

It was hypothesized that adding a toxin to IgG3-Av would increase the cytotoxicity of the antibody by facilitating a two-pronged attack against malignant cells. The *Saponaria officinalis* toxin saporin, which blocks protein synthesis by interfering with ribosomes, was selected for this effort. Annexin V staining showed that saporin-conjugated IgG3-Av is more toxic to cells than the unconjugated antibody. Additional experiments revealed that TfR targeting is required for delivery and cytotoxicity of saporin. Also, in contrast to unconjugated IgG3-Av, saporin-induced cell death is iron-independent. The conjugated antibody was found to block protein synthesis and activate a broad spectrum of caspases.

The current study involved gene expression profiling to evaluate saporin-regulated genes in the IM-9 and U266 cell lines, both of which are sensitive to saporin-conjugated IgG3-Av. A number of genes differentially expressed in both cell lines were identified, including HIST2H4, NFκBIE, and GADD45B. IM-9 cells are more sensitive to saporin and exhibited gene expression changes earlier and at a greater magnitude than in U266 cells.

This is the first time gene expression profiling has been used to evaluate saporin-regulated genes. Future experiments will include validation of these changes using RT-PCR, functional validation experiments, and evaluation of the *in vivo* cytotoxicity of IgG3-Av alone and conjugated to saporin in mouse xenograft models.

Isolated Dendritic-Cell-Specific Ligands for In Vivo Antigen Targeting

Tracy Diaz, UT Southwestern Medical Center

There are currently 250 clinical trials on ClinicalTrials.gov investigating cancer vaccines; of these, 60 are testing dendritic cell vaccines in lung, breast, cervical, or prostate cancer or multiple myeloma. There are several challenges associated with the development of cancer vaccines, such as identification of tumor-specific antigens and removal of negative immunological regulation (T_{reg} cells). Another major challenge is inadequate antigen presentation by antigen-presenting cells. In an attempt to address this issue, a screen was conducted to identify peptides that target and mediate internalization by dendritic cells (a type of antigen-presenting cells). A peptide-presenting phage display library identified 11 peptides associated with lung cancer cells, one of which binds to integrin $\alpha v \beta 6$. Biochemical approaches were used to identify other potential targets for vaccine development. Three different vaccination formats will be explored in a live tumor model: (1) genetic immunization, (2) targeting peptide-antigen conjugate, and (3) liposomes conjugated to targeting peptide.

Design and Synthesis of Novel Conformationally Restricted Peptides as Chemical Modulators for CBP Bromodomain

Guillermo Gerona-Navarro, Mount Sinai School of Medicine

p53 is a transcription factor that regulates cell cycle arrest, senescence, and apoptosis in response to stress or DNA damage. Functional activation of p53 requires acetylation of the protein on specific lysine residues. CREB binding protein (CBP), a transcriptional coactivator, has been shown to acetylate p53 on lysines 373, 382, 372, and 381. Acetylated lysine 382 serves as a binding site for the bromodomain (BRD) of CBP. The interaction between acetylated lysine 382 and the BRD of CBP that is responsible for p53's recruitment of CBP following DNA damage. Despite the importance of lysine acetylation to p53 function, the specific effects of single or combinatorial acetylation on different lysine residues remains elusive.

To explore the mechanisms of p53 regulation by lysine acetylation, chemical ligands with the ability to selectively modulate p53 interactions and activity were developed. Six novel conformationally restricted peptides that block the association of acetylated lysine 382 with the BRD of CBP were designed using Molecular Dynamics simulations. The peptides, all of which are cyclic, were synthesized using solid phase synthesis. After cleavage from the resin, the cyclization step was carried out by forming a disulfide bridge between two cysteine residues. Finally, using fluorescent polarization, the binding of these peptides to the CBP bromodomain protein was evaluated. These cyclic peptides have been used in cell-based assays to study cellular function of endogenous p53 and its effector proteins.

Anchorage-Independent Growth of Tumor Cells Is Mediated by Proteins That Are Concentrated in Serum Exosomes

Josiah Ochieng, Meharry Medical College

Most cells need to be attached to the extracellular matrix in order to grow; however, malignant cells acquire the ability to grow even when they are not attached to a matrix, a phenomenon called anchorage-independent growth. Anchorage-independent growth is just one of many transitions a cancerous cell undergoes; others include an epithelial-mesenchymal transition in cell morphology, loss of contact inhibition, and activation of new signaling pathways. Anchorage-independent growth can be studied in the laboratory using soft agar assays. Cell growth in soft agar mimics *in vivo* growth. Whereas the signaling pathways involved in anchorage-independent growth have been studied, little is known about serum factors (other than growth factors) that are involved in this process. Exosomes have been shown to mediate growth of cancer cells and may play a role in anchorage independence.

Exosomes are small vesicles secreted by most mammalian cells. They are used by cells to dispose of obsolete proteins and may also be a form of intercellular communication. Cells growing in soft agar were treated with either exosomes isolated from bovine or exosome-depleted serum. This experiment revealed that 90 percent of anchorage-independent growth was due to exosomal factors. A proteomics approach was used to identify proteins in serum exosomes. Some of the proteins had previously been identified in other types of exosomes while others appeared to be unique to bovine serum exosomes. One of the proteins found in bovine serum exosomes was fetuin-A. Interestingly, antibodies to bovine fetuin-A slowed the exosome-mediated anchorage-independent growth of tumor cells. Future experiments will explore the mechanisms by which exosomal fetuin-A mediates anchorage-independent growth directly or indirectly.

Concurrent Session II-2: Recruitment and Retention Issues

Moderator: Elizabeth Ness, Center for Cancer Research, NCI

Pilot Program for a Navigator to Increase Minority Enrollment Into Clinical Trials

Tracy A. Battaglia, Boston University Medical School

Only 2.5 percent of eligible patients enroll in cancer treatment trials; furthermore, minority populations are underrepresented in clinical trials. This underrepresentation threatens efforts to reduce the unequal burden of cancer in these vulnerable populations. Barriers to accrual of minority populations to clinical trials include fear, mistrust, and the narrow eligibility criteria of many trials. Patients are often deemed ineligible because of comorbidities or because they do not speak or read English.

The Minority-Based Community Clinical Oncology Program (MBCCOP) was formed to increase enrollment of underserved populations in clinical trials. These programs help minority populations access NCI-sponsored cancer prevention and treatment trials and have significant potential to increase minority clinical trial enrollment.

The NCI Patient Navigation Research Project is a multisite study currently underway. The goals of this program are to reduce delays in diagnosis and treatment among underserved populations. PNRP aims to reduce cancer disparities and targets vulnerable populations by identifying barriers to quality care. Patient navigation has the potential to bridge the gap that exists between MBCCOP trials and minority accrual.

The objective of this study was to demonstrate the feasibility and effectiveness of patient navigation in (1) promoting access to cancer prevention and control clinical trials and (2) increasing accrual of minority populations to clinical trials at inner-city academic medical centers. The study was conducted from January 2007 to March 2008 at Boston Medical Center (BMC), which has been a PNRP site since 2005. The hospital, which is the largest safety-net health institution in New England, serves low-income and inner-city residents; two-thirds of the patients are racial or ethnic minorities. The study resulted in implementation of patient navigation and a number of new cancer prevention trials at BMC. Minority accrual to these trials was measured by the number of eligible cancer patients screened versus the number of eligible cancer patients enrolled and the percent minority of both groups.

Pilot intervention was performed by a nurse navigator. Once the nurse navigator had been hired, both the navigator and the clinical trial office were trained. Training, which focused on identifying barriers for minority patients, was performed using monthly seminars as well as standardized and individual training. Electronic medical records (EMR) were used to identify and track eligible patients.

The patient navigator (PN) performed several activities aimed at increasing minority recruitment to available trials. First, the PN helped provide insight into the appropriate trials and identified eligible patients. The PN also worked with insurance providers. Face-to-face meetings were conducted to help identify barriers experienced by patients being enrolled in a clinical trial, and the navigator performed tracking and follow-up once initial meetings had taken place.

BMC reviewed all currently active Division of Cancer Prevention trials and initiated a collaboration with the Cook County MBCCOP in order to identify clinical trials with which it could be involved. These searches located trial E2 Z02, Symptom Outcomes and Practice Patterns. This trial, which is led by the Eastern Cooperative Oncology Group, is a survey of disease and treatment-related symptoms of invasive cancer from the breast, prostate, lung, or colon/rectum.

Between October 2007 and March 2008, 62 patients were approached for enrollment in the E2 Z02 trial. Of these patients, 21 were ineligible, mainly because of their inability to speak or read English. Forty-one patients were eligible, and 35 were enrolled in the trial. Of those enrolled, 62 percent were Caucasian, 35 percent were African American, and 3 percent were African American/Hispanic. Nearly half of the enrolled patients (47 percent) had either no health insurance or were enrolled in Medicaid. Twenty-nine percent had private insurance, and the remaining 24 percent were covered by Medicare.

Analysis of the program indicated patient navigation is a viable model to increase accrual of minority populations to cancer clinical trials. It also highlights the need for trials with broader eligibility requirements. The use of EMR was identified as a promising method for identifying and tracking eligible patients.

This program will continue to be used as a supplement to the Boston PNRP, and plans are in place to open two new trials over the next twelve months. In order to better identify and track patients, EMR tools will be refined. BMC has applied for the MBCCOP and plans to expand navigation and involve community health centers to help increase enrollment of minority and underserved populations in clinical trials.

Enhancement of Recruitment of African Americans to National Oncology Clinical Trials

Debra Wujcik, Vanderbilt University

In 2001, the Meharry-Vanderbilt Cancer Partnership used a U54 grant to establish an oncology clinic at Nashville General Hospital on the Meharry Medical College (MMC) campus. The partnership was awarded an MBCCOP grant in 2003. These resources have enabled the partnership to recruit more African Americans to national clinical trials.

A number of factors that hinder minority patients from accessing medical care and participating in clinical trials have been identified. These include missed appointments, failed communication, unreliable transportation, lack of insurance, and lack of health literacy.

All patients diagnosed with cancer at MMC are evaluated for clinical trial eligibility. Patient pathology reports are sent to research staff, who notify the treating physician if a patient may be eligible for a research study. All eligible patients are given the opportunity to participate in a trial, even if they lack resources (e.g., transportation, insurance). Accrual rates for African Americans within the program have ranged between 40 and 58 percent since 2001; these rates are far higher than the national average. Factors that prevented patients from participating in clinical trials have included co-morbidities, lack of eligibility, refusal of treatment, and refusal to participate.

The protocols being conducted at the clinic are periodically reviewed to identify gaps in the protocol portfolio. Potential new studies are identified, in part through Cooperative Groups, and studies are prioritized based on the patient populations they target.

Between 2005 and 2007, 556 patients were screened for cancer at MMC. Of these, 46 percent were black, 45 percent were white and 8 percent were Hispanic. Approximately one-quarter of the patients were covered through Medicare or Medicaid and 38 percent were uninsured. Overall, 30 percent of eligible patients for whom an appropriate study is available have been enrolled to a clinical trial.

Plans are in place to hire a translator and translate consent form to help recruit non-English speaking patients. Hispanics account for 7 to 8 percent of the population of Davidson County, where Nashville General Hospital is located. A process is also underway to allow inmates in the Tennessee correctional system to participate in clinical trials. Approval has been obtained from the IRB and the Department of Corrections Commissioner.

In summary, the program at MMC has shown that many racial and ethnic minorities and underinsured patients are willing to participate in cancer clinical trials if given the opportunity. A team approach to clinical trials and case management strategies (i.e., patient navigation) help ensure successful recruitment and retention.

Relationships Among Race, Cancer Knowledge, Available Sources of Medical Information, and Perception of Cancer Treatment: A URCC CCOP Study

Pascal Jean-Pierre, University of Rochester Medical Center

Illness knowledge and sources used to obtain information about cancer can influence a patient's health behaviors, but few studies have examined the effects of these variables on the perception of cancer treatment across different ethno-cultural groups.

The effects of patients' knowledge on their perception of treatment were studied in a group of 973 patients undergoing cancer treatment at 20 geographically separate Community Clinical Oncology Program (CCOP) affiliate sites. The group consisted of 904 white and 69 nonwhite patients. Participants provided information about their perceptions of cancer and cancer treatment as well as the sources they used for cancer information (e.g., medical, professional, community, or media).

Examination of the responses revealed that there is a significant relationship between a patient's race and utilization of medical or professional sources for cancer information as well as their perception of cancer and its treatment. Nonwhites reported a greater desire for cancer-related information and were less likely to rely on medical and professional information sources. No significant difference in education or occupation was revealed between white and nonwhite participants. A multiple regression analysis of the data revealed a significant model that explained 82 percent of the variance in patients' perceptions of cancer treatment. Knowledge of the illness and use of medical or professional sources for information strongly predicted perception of cancer treatment.

This study demonstrates that race is a factor in the unmet need for cancer information and that patients from different ethno-cultural groups use different sources for this information. It appears that programs designed to enhance patient knowledge of cancer and its treatments are not adequately reaching racial and ethnic minorities. These results suggest that clinicians working with patients from diverse backgrounds need to assess patient understanding of cancer and desire for more information.

Factors Associated With Retention of African-American Women

Monica Baskin, University of Alabama at Birmingham

Physical activity plays an active role in the prevention and control of cancer. It has been shown that both vigorous and moderate levels of physical activity can lower the risk of certain types of cancer, and regular physical activity improves quality of life among cancer patients and survivors. However, most adults in the United States fail to meet current recommendations of at least 30 minutes of moderate-intensity physical activity on 5 or more days per week. Women who live in the Deep South are even less likely to adhere to these recommendations. Therefore, efforts to engage African-American women in regular physical activity has implications for cancer prevention and control, but there are ongoing challenges with both recruitment and retention of these women to long-term physical activity programs.

There are only a limited number of published studies on the factors associated with retention of African-American women in long-term, population-based physical activity interventions. This study attempts to examine whether demographics, health behavior, and/or health status can predict retention of women engaged in a community-based walking program six months after initiation of the program.

Study data were collected by Deep South Network for Cancer Control volunteers. These volunteers are made up of both Community Health Advisors as Research Partners and Community Network Partners. Walk teams were made up of two or more walkers across 22 counties. Walkers received a starter kit with a t-shirt, pedometer and a wrist band, and each walker was taught how to record daily steps. The Deep South Network volunteers collected and submitted team members' step data each month.

A wellness questionnaire was used to collect information on each participant's overall physical health, any prior diagnosis of a health condition, cancer-screening history (e.g., mammogram, clinical breast exam, breast self-examine, pap-smear), physical activity, fruit and vegetable intake, and demographics. The questionnaires were administered at the beginning of the program and at six and twelve months.

A total of 1,256 African-American women enrolled in the walking program, and 77 percent of these women continued to participate at six months. Responses to the wellness questionnaire were used to identify predictors of retention, which included marital status, employment, education, clinical breast exam, breast self-exam, and Pap smear.

This study has helped identify factors that affect retention of women in organized activity groups. For example, having CNPs act as WALK team leaders and motivators provides social support that may be instrumental in retention, particularly of women who begin the program without a partner. The WALK program is part of a comprehensive cancer prevention initiative, and retained walkers may represent women who have benefited from previous outreach (e.g., breast and cervical cancer screenings).

Challenges in retaining employed women are likely due to difficulty scheduling walk times around work schedules.

There are also several challenges inherent to a program of this type. The model relies on an infrastructure of volunteers to provide leadership and social support. It is also necessary to sustain community interest in the program and improve participant-centered data collection methods.

To further understand the factors involved in retention, steps will be taken to better characterize specific retention strategies by team leaders with high and low retention. The study findings and an ongoing assessment of retention at 12, 18, and 24 months will be used to tailor retention activities and inform future programs.

Concurrent Session II-3: Role of Physical Activity and Nutritional Factors in Cancer Health Disparities

Moderator: Jackie Whitted, Division of Cancer Prevention, NCI

Establishing a Community-Based Program for Physical Exercise (WALK) Suitable for Low-Income Residents

Mona Fouad, University of Alabama at Birmingham

Obesity is a risk factor for developing cancer, and a sedentary lifestyle contributes to obesity. States in the southeastern United States have the highest rates of obesity in the country. Experts say simply walking for one hour a day can add two years to a person's life. The purpose of this study was to establish a community-based program for physical activity that is accessible to low-income people. The goal was to create a low-cost, flexible, easy-to-implement community empowerment program.

This CNP study targeted ethnic minorities and low-income groups in Birmingham, Alabama. The program, called WALK, was implemented in four phases: first, in Birmingham, then expanded to Jefferson County, then to counties with high concentrations of African-Americans, and finally statewide. Participants registered through a program Web site and participated on one of three levels: as a team captain, team member, or walker. Those who were chosen as team captains were generally community leaders who already exercised regularly. They were trained regarding how to motivate their teams, which consisted of up to ten people.

The program also partnered with community leaders and other stakeholders to create community coalitions, establish neighborhood walking teams, train captains, create the Web site (which could also be used for participants to self-report their steps using a pedometer), and establish a rewards system as an incentive to accumulate steps. As a result of a specific partnership with the Birmingham mayor, WALK became part of the Healthier Birmingham platform. Furthermore, the Deep South Network for Cancer Prevention and Control also adopted the program, allowing it to move beyond state lines.

After six months, 77 percent of individuals and 198 of the original 210 teams were still active. Qualitative interviews were conducted with team captains to determine which strategies were effective (more than 70 percent participant retention) and which were not (less than 70 percent participant retention). Later, the Web-based self-reporting mechanism was abandoned in favor of scannable forms, because participants were not using the technology.

In conclusion, the WALK program is efficient and sustainable in urban and rural areas; it can also be replicated in other hard-to-reach areas of the United States. In the future, the researchers would like to expand the WALK program throughout the South and to the Hispanic community.

Healthy Lifestyle: A Community-Based Nutrition and Physical Activity Behavior Change Intervention Program

Vivian Carter, Tuskegee University National Center for Bioethics in Research and Health Care

The Healthy Lifestyles program is implemented by the Morehouse School of Medicine/Tuskegee University/University of Alabama at Birmingham Comprehensive Cancer Center Research Partnership in collaboration with the Macon County Community Health Advisors. The aim of the program is to develop and evaluate culturally sensitive programs to promote healthier lifestyles and reduce the risk of cancer. The goal is to engage multiple levels of the community to produce a sustainable program that lasts beyond the scope of the current project. This program is specifically designed to target African Americans in rural Alabama. It targets individuals, community organizations, and policy makers to address cancer risk reduction by promoting healthy eating and physical activity. The primary objectives are to improve access to and use of nutritional and physical activity programs and to change attitudes, knowledge, and practices regarding the use of helpful programs and the discontinuation of harmful behaviors.

Five focus groups were held with a total of 34 local participants, most of whom reported annual incomes of less than \$25,000. Surveys of these groups revealed that 72 percent of the participants had tried dieting to lose weight, and 43 percent had tried diet products like laxatives and diuretics and diet pills. A large majority of the participants (85 percent) felt as if they needed to lose weight and most of these indicated that exercise was the best way to do so. Only 36 percent of the participants rated their health as “good.”

The program then chose volunteer team leaders who resided in Macon County and had not previously participated in a research study. These leaders completed an 8-week educational nutrition course that included information on cancer and nutrition. The team leaders also helped the program coordinators recruit volunteer participants from the community. Individuals were instructed to change their diets and to exercise (at Curves gym, by doing floor aerobics, tai chi, walking, or water aerobics).

Participants in the program reported a decrease in weight, blood pressure, and measurements (taken at the waist and at the bust). The program encouraged individuals to exercise and help the community by participating in a walking trail-cleaning day, the Health Marathon for Cancer Awareness and Prevention, Relay for Life, and the Alabama Department of Public Health’s New Leaf program.

Dietary Practices of African Americans in Macon County, Alabama

Adelia Bovell-Benjamin, Tuskegee University

In the United States, African-American males have higher cancer incidence and mortality rates than white males. African-American females have a lower incidence of cancer but still higher mortality rates than white women. Bad nutrition contributes to these disparities, as poor diet is a risk factor for cancer. The most commonly used dietary assessment instrument is the Food Frequency Questionnaire (FFQ), a semi-quantitative method that requires users to recall their food consumption over a specific period of time. The NCI Dietary Health Questionnaire is a commonly used FFQ, as it has been extensively studied and validated in the United States. However, there is not much information regarding its validity for African Americans in the rural South, and there have been only limited attempts to develop more culturally sensitive FFQs for use in the southeastern United States. One questionnaire was developed for the lower Mississippi Delta in 2005, wherein researchers reported regional food patterns that differed from national patterns and between whites and African Americans in the same region.

The current study generated information about dietary practices and food preferences among African Americans in Macon County to inform the creation of a modified FFQ. It utilized focus groups, as they are good tools for understanding dietary habits of African Americans. The study used other strategies as well, including literature reviews and brainstorming with African-American faculty and staff. The researchers compiled a focus group interview guide and conducted two pilot and eight formal focus groups, which were audiotaped and transcribed verbatim.

Typical breakfast foods were reported by the focus groups and fast food, ham, turkey, and bologna sandwiches were the most common lunch foods. The most common food preparation method was frying. These results indicate that the modified FFQ should include fried cornbread, cornbread in buttermilk, fried green tomatoes, succotash, rutabega, and turnip greens. Conversely, it should not include fajitas, enchiladas, quesadillas, turkey nuggets, and liverwurst. African Americans generally prefer traditional foods representing a large part of their cultural history. “Soul food,” which includes greens, okra, fried green tomatoes, potato salad, macaroni and cheese, corn, pork products, and chitlins, is widely perceived to be healthy and inexpensive.

In summary, the unique dietary habits of African Americans should be taken into consideration when creating or modifying assessment tools. The modified FFQ that resulted from this study must be tested and validated for use with African Americans in the rural South.

Designing Healthy Worksites

Jodi Leslie, 'Imi Hale-Native Hawaiian Cancer Network

Native Hawaiians have a high rate of obesity, which is a risk factor for cancer. Worksite wellness programs have been shown to improve health behaviors on an individual basis. The purpose of this research is to gather data from administrators and staff of Hawaiian-serving organizations. These data will be used to develop programs and policies for healthy workplaces.

To this end, the study recruited eight Hawaiian-serving organizations, including churches, social service organizations, and advocacy agencies. Site visits, interviews with management, focus groups for administrators and staff, and online employee surveys are being used for data collection. The surveyors asked management about their resources, policies, and support for healthy worksites. Employees and staff were also asked about their preferences for programs. Site tours were used to evaluate open space (for exercise classes), presence of stairs and sidewalks, availability of a kitchen area, and the availability of health options in vending machines. Measurements of success for programs will include body mass index (BMI), weight, and measures of happiness and well-being. So far, findings suggest that site managers are enthusiastic about participating in the research, and workers are willing to have physical measurements taken to track progress. These findings will be used to design and pilot test healthy workplace programs.

Diet and Obesity Among Adults in Guam

Rachael T. Leon-Guerrero, University of Guam

In Guam, cancer is the second-leading cause of death. The Chamorro, who are indigenous Pacific Islanders, have the overall highest age-adjusted mortality rate due to cancer in Guam. The most common cancer sites are lung for men and breast for women. In Guam, 37.6 percent of the people are overweight, and 23.3 percent are obese. The traditional Chamorro diet included taro, breadfruit, yams, cassava, coconut, and fish, but after WWII the diet shifted to include imported rice and canned foods. Celebrations and sharing food are very important elements of Chamorro culture.

This study compares the dietary intakes of the Chamorro and Filipino populations in Guam, using 24-hour recall to measure intake of certain foods. There were 127 participants in the study, evenly distributed by gender and Chamorro versus Filipino. The Chamorros were significantly more obese than the Filipino participants, and had higher BMIs. The study found that Chamorros consume more calories from sugary beverages and also eat more fat and sugar and less fiber. The findings also indicate that Chamorros do not consume enough fruits and dairy products.

Key Points of Discussion—Session II-3

- v In the Tuskegee study, participants were allowed to choose the program they wanted to join. They were required to commit to being in the program for 2 years, so they had to choose something they could commit to as a lifestyle change. There were 5 team leaders and 5 persons per team.
- v Many of the foods described by the Tuskegee investigators as “soul food” have a high fat content before they are prepared, and thus are not generally considered to be healthy choices.
- v In Guam, Chamorros were found to have a higher incidence of diabetes than Filipinos. However, the number of Chamorro participants was too small to be considered representative.
- v Because of the westernization of culture in Guam, many locals have a negative attitude about local foods, many of which provide healthy alternatives.

Concurrent Session II-4: Signal Transduction of Cancer (II)

Moderator: Nelson Aguila, Diversity Training Branch, CRCHD

Focal Adhesion Kinase Mediates Adhesions and Cell Spreading of Bone-Metastatic Breast Carcinoma Cells

Edna Mora, UPR Comprehensive Cancer Center

Metastasis of primary tumors is a complex process. Two critical steps of this process are cell adhesion and spreading. FAK has been identified as one of the most important proteins in the metastatic signaling cascade. FAK is activated upon binding of integrins at the cell membrane and subsequent tyrosine-phosphorylation by Src kinase. Once activated, FAK affects several different downstream pathways that modify growth, cell adhesion, migration, chemotaxis, cell spreading, angiogenesis, and apoptosis.

Recently, a new therapeutic concept called anti-adhesion therapy has been proposed for several primary tumors. This adjuvant therapy targets the increase in expression of FAK in malignancies such as brain, breast, prostate, pancreatic, liver, gastric, lung, ovarian, head and neck, and esophageal tumors. However, the role of FAK in human bone metastases has not yet been evaluated.

Bone metastases are a large concern for patients with breast cancer. Bone is the most common distant metastatic site in breast cancer patients, and 70 percent of patients will develop bone disease. There is currently no curative treatment for bone metastases, which cause a high morbidity rate.

In order to study the effect of FAK on bone metastases, a bone-metastatic cell line was created by intracardiac injection of mice with a breast-tumor cell line (MDA-231). After six to eight weeks, bone metastases occurred, and tumor cells were isolated and reintroduced by intracardiac injection. The result was a bone-seeking cell line derived from MDA-231 cells. Western blot analysis revealed that the bone metastatic cells had a significant overexpression of FAK compared to parental cells.

To determine if overexpression of FAK promotes adhesion and spreading of bone-metastatic breast carcinoma cells, adhesion and cell spreading assays were performed on the new cell line. Adhesion was measured by crystal violet assay, and cell spreading was evaluated microscopically to detect decreased light halo, membrane budding, or spreading. The adhesion assays showed that coating wells with collagen I, gelatin, defined matrix, or fibronectin increased adhesion of bone-metastatic MDA-231 cells. Collagen and fibronectin both stimulated cell spreading of bone-metastatic cells, and, in this case, spreading was similar at both early and late timepoints.

To further define the role of FAK in bone-metastatic cells, FAK expression was inhibited using siRNA techniques. After treatment with siRNA FAK, there was a significant decrease in adhesion to both collagen and fibronectin. A similar result was observed for cell spreading. These results suggest that

inhibition of FAK is able to decrease cell adhesion and spreading of bone-metastatic breast carcinoma cells and that therapies targeting FAK expression could help to limit metastases of breast tumors.

Key Points of Discussion

- v In the ovarian studies, the investigators examined several FAK phosphorylation sites.
- v Among breast and ovarian cancer patients, prognosis is worse when FAK is expressed.

Role of Leptin Signaling in Mammary Tumor Progression

Ruben Rene Gonzalez-Perez, Morehouse School of Medicine

Leptin is primarily known for its role in the regulation of energy balance and appetite, but it is also involved in reproductive processes, angiogenesis, cell proliferation, inflammation, and anti-apoptosis. Recently, elevated levels of leptin have also been associated with increased incidence and poor prognosis in breast cancer cases.

Leptin is a small, helical cytokine predominantly secreted by adipocytes. Leptin is a product of the obese gene (OB), and interacts with the leptin receptor (OB-R). Binding of leptin to OB-R stimulates the JAK2-STAT3 pathway, which is thought to regulate the apoptotic, proliferative, and angiogenic actions of leptin. Because of its role in cell growth, the actions of leptin have also been implicated in the progression of cancer, and it is possible that disruption of leptin signaling will negatively impact mammary tumor growth by decreasing leptin-induced expression of pro-angiogenic, proliferation, and anti-apoptotic factors.

To determine if it is possible to disrupt leptin signaling through the OB-R, two leptin peptide receptor antagonists (LPrA) were designed based on the crystal structure of another helical cytokine, G-CSF, bound to its receptor, G-CSF-R. Structural alignment of G-CSF with leptin identified the potential OB-R interaction site on the protein. The LPrA molecules were modeled from helix 1 (LPrA1) and helix 3 (LPrA2).

The effects of LPrA1 and 2 on angiogenesis were measured using the chicken chorioallantoic membrane assay. In contrast to tissue treated with PBS and a control peptide (LPrASc), capillary formation was inhibited by both LPrA1 and LPrA2. This effect was found to be dose-dependent, and indicates that inhibition of leptin signaling disrupts angiogenesis.

The effect of the peptide antagonists on mammary cancer cells was also determined. When treated with leptin, breast cancer cells showed an increase in adhesion and proliferation due to signaling through the OB-R. However, when cells were treated with a combination of leptin and LPrA2, there was a decrease in the percent of proliferation and adhesion in three different cancer cell lines. Treatment with the control peptide, LPrASc, did not have an effect on the adhesion or proliferation of the cells.

The pharmacokinetics of the peptide LPrA2 were measured in mice. Unconjugated peptide had a half-life of approximately one hour after intraperitoneal injection. Addition of an N-terminal PEG group to the peptide (PEG-LPrA2) increased the half-life in mice to 18 hours. Different modes of injection (e.g., intravenous, subdermal, and vaginal) were able to further increase the half-life of the pegylated form of the peptide, and a dose of 53.570 mg/kg by vaginal injection had a half-life of 128.8 hours.

The role of leptin in the regulation of energy and appetite makes it possible that there would be adverse side effects upon inhibition of the OB-R pathway. Examination of the central nervous system showed no accumulation of LPrA2, which suggests that appetite would not be affected. Observation of the study subjects showed no change in food intake, body weight, glucose levels, insulin serum levels, or the HOMAX-index.

Determination of the effect of LPrA peptides on breast cancer was examined using a mouse model and two human xenograft models. In the first experiment, BALB/c syngeneic sisters were injected twice daily

with m4T1 tumor cells and PEG-LPrA2. Next, ovariectomized and estrogen-supplemented SCID mice were treated with LPrA2 before and during inoculation with MCF-7 tumor cells. Finally, human MDA-MB231 cells were injected into SCID mice that had been pretreated with PEG-LPrA2. In all cases, preventive treatment with LPrA2 delayed the onset of tumor growth and also caused a large reduction in the volume of the resulting tumor. In the case of MCF-7 cells, tumor growth was delayed by three full weeks. When LPrA2 treatment was started after tumor formation, the volume of the tumor was significantly reduced in all three models. Examination of the tumors themselves showed a decrease in the expression of the OB-R downstream-effectors vascular epithelial growth factor (VEGF) and the VEGF receptor. The levels of several other signaling molecules were also reduced in MCF-7 cells and MDA-MB231 cells (e.g., interleukin-1 [IL-1], IL-1 receptor, Bcl-2, CD31, CD68, leptin, and OB-R).

Examination of signaling pathways in m4T1 cells treated with LPrA2 showed that the peptide is able to block canonical leptin signaling and downregulate SOCS3. Normally, leptin activates the ERK1/2/MAPK, PI3K/AKT1, and JAK2/STAT3 pathways. Application of LPrA2 reduced phosphorylation of these proteins to basal levels in the presence of leptin.

m4TI cells were also used to further define the signaling pathway downstream of the VEGF receptor (VEGFR2) after exposure to leptin. Cells were treated with leptin and the levels of VEGF, VEGFR, and cyclinD1 were determined. Exposure of leptin-activated cells to AG490, Wortmannin, and PD98059 showed that STAT3, PI3K, MAPK, and ERK1/2 are important components of leptin signaling through VEGFR2. Further studies of signaling from the VEGFR were performed with truncated versions of the protein. Five different constructs were made, and the protein interaction sites for HRE, AP1, AP2, NFκB, and SP1 were sequentially removed. The constructs were expressed in m4T1, MMT, and EM6 cells. The preliminary results suggest that SP1 could be a positive regulator of VEGFR in m4T1 and MMT cells. These studies suggest the pathway by which leptin can increase VEGFR signaling. Once JAK2 is activated by leptin binding to the OB-R, signaling progresses through PI3K and MAPK. PI3K then stimulates mTOR, HRE, AP1, NFκB, and SP1, which upregulate VEGF. MAPK can either directly affect HRE, AP1, NFκB, and SP1 or activate them indirectly through IL-1β and IL-1Rtl.

In conclusion, a region of leptin that interacts with the OB-R was identified by structural comparison with another cytokine. The subsequently designed leptin peptide receptor antagonist has been shown to decrease mammary tumor growth by inhibiting leptin-induced mitogenic, angiogenic, and anti-apoptotic effects. Upon inhibition of leptin binding to OB-R, downstream signaling was disrupted and tumor growth slowed. These effects were more pronounced on mammary tumors that are estrogen receptor positive than those that are estrogen receptor negative.

Key Points of Discussion

- v Histological differences were detected between experimental and control patients.
- v The investigators plan to address additional questions about this pathway, including whether Bcl-2 induces VEGF.

Prognostic Significance of p53 Codon 72 Polymorphism Differs With Race in Colorectal Adenocarcinoma

Venkat Katkooi, University of Alabama at Birmingham

There is a multi-step, molecular pathway to the onset of colorectal cancer (CRC). After many decades, normal epithelial tissue forms abnormal crypts foci. This leads to early adenoma and late adenoma after two to five years. An *in situ* carcinoma then forms, and after 2 to 5 years, an invasive carcinoma develops. Eventually, this pathway leads to a metastatic carcinoma. Many of the genes responsible for this transformation have been identified, and the changes in gene function can occur via either the chromosomal instability pathway, which includes gene mutations and chromosomal deletions, or through

the microsatellite instability pathway, which occurs through mismatch repair inactivation. Two prognostic markers have been identified for sporadic colorectal adenocarcinoma, microsatellite instability and 18q deletion. Several more candidate prognostic markers have also been identified (e.g., p53, p27^{kip-1}, Bcl-2, Bax, MUC1, and Rabphilin-3A-like (RPH3AL)). The prognostic value of each marker differs based on the tumor location, tumor stage, and/or the patient's race or ethnicity. This study aims to identify race-specific prognostic molecular markers in CRCs by evaluating mutational patterns of the p53 gene and correlating the mutations with patient outcomes based on race.

Three hundred seventy-three patients who underwent surgery with curative or palliative intent at the University of Alabama-Birmingham (UAB) during 1985 to 1995 were selected for the study. Of the 373 patients, 137 were African Americans and 236 were non-Hispanic Caucasians. Both CRC and corresponding normal tissue was collected from each patient. None of the patients received any pre- or post-surgery adjuvant therapy. Patients with a family or personal history were excluded. Patient demographical, pathological, and clinical information was extracted from medical records and physicians' charts. Any follow-up information was collected from the UAB Tumor Registry.

Microsatellite instability was analyzed by ABI and Light Cycler at BAT25, BAT26, D2S123, D5S346, and D17S250 in 373 CRCs and the matching normal tissues. The results indicated no significant difference in microsatellite instability between African-American patients and Caucasian patients.

In order to determine the potential of p53 as a prognostic marker, sequence analysis was performed on exons 4 to 9 of p53. The analysis showed a similar overall frequency of mutations between African-American and Caucasian patients. Mutation of p53 was associated with poor survival rates in both races.

Next, an analysis was performed of the occurrence of the single nucleotide polymorphism located at codon 72 in p53 that results in the substitution of arginine for proline. This amino acid change leads to increased degradation of p53 and increased tumorigenicity and oncogenic effect. This polymorphism has also been shown to lead to uncontrolled malignant process and increased invasiveness and metastasis. Risk of cancer progression, poor prognosis, and resistance to anticancer therapy has also been observed in patients with this particular p53 polymorphism.

Restriction fragment length polymorphism analysis and sequencing were used to analyze the genotype status at codon 72 of p53. Three phenotypes were identified: Arg/Arg phenotype (G/G homozygous), Arg/Pro phenotype (G/C heterozygous), and Pro/Pro phenotype (C/C homozygous). The Pro/Pro phenotype is correlated with a nodal metastasis tumor grade and has a higher incidence in African-American patients.

The prognostic value of this polymorphism (Pro/Pro) was evaluated in relation to the other phenotypes (Pro/Arg and Arg/Arg) based on race. A survival analysis based on phenotypes of codon 72 polymorphism by race showed that the Pro/Pro phenotype is associated with poor survival only in African-American patients and not in Caucasian patients. A Cox regression was then used to determine the prognostic significance of p53 codon 72 phenotypes. The Pro/Pro phenotype is an independent prognostic marker only in African-American patients with CRCs. Investigation of the mutational spectra of p53 showed that the Pro/Pro phenotype is associated with a higher frequency of other particularly disruptive p53 mutations only in African-American patients.

In summary, the p53 mutational pattern and prognostic value of codon 72 polymorphism differs with race in colorectal adenocarcinomas. The incidence of the Pro/Pro phenotype at codon 72 of p53 is higher in African-American patients and is associated with a higher incidence of p53 mutations. The Pro/Pro phenotype is associated with a poor clinical outcome for African-American, but not Caucasian, patients with CRCs.

Key Points of Discussion

- v When the investigators correlated with microsatellite instability status, they did not identify any differences between Caucasian and African-American patients.

avb3 Integrin-Ligand Binding Is Regulated by Protein Kinase A

Annette Gonzalez, Northwestern University

In order for angiogenesis to occur, endothelial cells must be able to traverse the extracellular matrix that surrounds them. An activated endothelial cell secretes matrix metalloproteinases that digest the surrounding matrix, allowing for cell migration and division. Integrins are heterodimeric cell surface receptors for matrix proteins that are activated by both external signals (outside-in signaling) and cytoplasmic signals (inside-out signaling). The complex interactions between endothelial cells and matrix ligands are in part regulated by crosstalk between $\beta 1$ integrin-containing heterodimers and $\alpha v\beta 3$ integrin. The integrin $\alpha v\beta 3$ has been shown to be activated by $\beta 1$ integrin, but the molecular mechanism that regulates this is unknown.

Laminin 411 is an extracellular matrix protein that binds to both the $\alpha v\beta 3$ and $\alpha 3\beta 1$ integrins. Solid phase binding studies revealed that the two integrins do not compete with one another for binding to a truncated form of laminin ($\alpha 4LN$), suggesting that they bind to distinct sites of the protein. Cell adhesion assays in the presence of either $\beta 1$ or $\alpha v\beta 1$ integrin function-blocking antibodies reveal that both $\alpha v\beta 3$ and $\beta 1$ integrins are required for endothelial cell adhesion to laminin (i.e., one cannot compensate for the other). However, in the presence of manganese chloride, which activates integrins independent of intracellular signaling, the function-blocking antibodies could not prevent adhesion. These results indicate that intracellular signaling allows $\beta 1$ integrin to activate $\alpha v\beta 3$.

Since the cell adhesion studies were performed with a truncated version of laminin, the ability of $\alpha v\beta 3$ to bind to another integrin ligand, vitronectin, was assessed. Cells were treated with antibodies that block the binding of endothelial cells to vitronectin as in the above experiment. Addition of $\beta 1$ function-blocking antibodies, $\alpha v\beta 3$ function-blocking antibodies, and a combination of both inhibited cell adhesion. However, addition of manganese chloride had an effect similar to the binding of $\alpha 4LN$, which suggests that the crosstalk observed between $\beta 1$ and $\alpha v\beta 3$ is not limited to a $\alpha 4LN$ binding and can occur with other ligands of $\alpha v\beta 3$.

Immunoprecipitation and western blot analysis revealed that serine phosphorylation of $\beta 3$ integrin increases five-fold when $\beta 1$ integrin function is blocked. Previous studies have shown that serine 752 of $\beta 3$ integrin is necessary for the conformational change to the high affinity ligand binding state. Alanine and aspartic acid substitutions at residue 752 were used to determine the effect on $\alpha v\beta 3$ ligand binding. S752A, but not S752D, was able to bind to $\alpha 4LN$, which suggests that phosphorylation on serine 752 inhibits cell adhesion by $\alpha v\beta 3$.

Additional experiments showed that in the presence of the $\beta 1$ integrin function-blocking antibody, activity of the kinase PKA was increased. Inhibition of PKA activity prevents the $\beta 1$ integrin function-blocking antibody from reducing the binding activity of $\beta 3$ integrin. This indicates that PKA is an intermediate that links the activities of the $\beta 1$ and $\beta 3$ integrins. Cellular phosphatases were implicated in this signaling cascade as well by experiments showing that treatment with phosphatase inhibitor calyculin A blocks binding of $\alpha v\beta 3$ integrin to $\alpha 4LN$. It was subsequently discovered that blocking $\beta 1$ integrin activity resulted in increased phosphorylation (activation) of phosphatase inhibitor 1, an inhibitor of protein phosphatase 1 (PP1), in a PKA-dependent fashion. Furthermore, blocking PP1 function pharmacologically inhibits $\alpha v\beta 3$ -mediated cell adhesion to $\alpha 4LN$ when both PKA and $\beta 1$ function are inhibited.

Together these data suggest a novel mechanism by which $\beta 1$ integrin modulates $\alpha v\beta 3$ integrin ligand binding. When $\beta 1$ integrin is inactivated, PKA phosphorylates/activates inhibitor 1, which in turn inhibits the activity of PP1. Inhibition of PP1 results in accumulation of serine phosphorylated $\beta 3$ integrin, which is unable to bind ligand.

Concurrent Session II-5: Promoting Cancer Awareness and Education Through the Use of New Media

Moderator: George Strait, National Center on Minority Health and Health Disparities, NIH

New media can provide researchers with better tools for obtaining the information they need. For example, a researcher studying obesity and diabetes in border areas found that the best way to conduct follow-up was sending text messages, because almost all of the project's clients had cell phones.

“New” Media Trends

Susannah Fox, Pew Internet Project

The Pew Internet Project, funded by the Pew Charitable Trust, is designed to study the social impact of the Internet using primarily telephone surveys. An important audience for the projects is grant writers who need data to support their hypotheses and emphasize the need for their proposed studies.

The project has identified several interesting trends in the social impact of new media. Two examples :

- v During the 2008 primary elections, voters paid more attention to political campaigns than they have usually paid to the fall elections in past years. The public is using the Internet to obtain “industrial strength” information rather than the consumer-oriented, prepackaged information offered by news media—they are reading speeches and position papers instead of press releases and edited interviews.
- v A story about a 4-year-old girl who was seen looking behind her family's television set provides an anecdotal illustration of the impact of the Internet. Her father thought she was looking for the characters represented inside the box; she explained that she was looking for the mouse.

The Pew Internet Project has developed a scale called a “thermometer of access” to the Internet. The high end of the scale is affluent, young, and predominantly white, while the lower end is older and has less income and lower educational levels. The project has published a report on the typology of individuals along the thermometer's scale in terms of technological assets and attitudes toward those assets.

Categories of technology users have been described; the “mobile-centric” category, for example, uses the cell phone like a Swiss Army knife for multiple purposes.

Eliminating Cancer Disparities in the Black Community: New Media Is the Answer

Johnny Taylor, RushmoreDrive.com

RushmoreDrive.com has developed an ethnically themed Internet search engine targeting the African-American community. The company views the Internet not as a new medium but as a new way to distribute information. Search engines are designed to deliver relevant information; RushmoreDrive.com uses a combination of general and vertical searching concepts to find relevant information for its target population. The service supports searching based on shared identity among members of the African-American population.

The most frequently searched Internet topic among African Americans is health care. African Americans experience health issues, including cancer, differently from other identity groups. RushmoreDrive.com is concerned, not only with tailoring Internet searches to the specific needs and interests of the African-American community, but also to ensuring that access is not limited to those who own computers.

Cancer Has Crept Among Us

Don Warren, Inter Tribal Council of Arizona

Mass communication is often ineffective among members of populations that are not part of mainstream society, such as those living on reservations. Cancer is a growing concern among Native Americans, but there are not enough Native Americans delivering information about cancer. When community members share their stories, fear is reduced. This type of communication is part of a researcher's translational responsibilities. Samples from two DVDs developed by the Southwest American Indian Collaborative Network CNP were shown to illustrate how this project is using new media to help native people tell their own communities about their cancer experiences.

Through the Native Looking Glass—Visual Images and Storytelling as Innovative Tools in a Regional Native Cancer Control Program

Brenda Manuelito, University of Washington

The Native People for Cancer Control project considers participatory medicine to be a way to humanize the health care system. The project is using “visual story telling” as an educational method. Visual story telling gives voices and power to communities and their members. It expands the concept of “access” beyond searching the Internet by using new media to improve health in the community. These activities are cost-effective using Moviemaker software on PCs. Ms. Manuelito shared several video clips illustrating the effectiveness of visual story telling.

Using New Media to Promote Cancer Awareness to the Internet Generation

Renee Turner, Black Entertainment Television

Black Entertainment Television (BET) has been successful in using new media to simplify complicated messages for younger audiences—for example, using a game show format to promote AIDS education. Young people will not take information seriously unless they can understand its significance for them. Stories must include people who look like them. BET also uses messages from celebrities of interest to young people as a link to vital information sources.

Because so many young people now own iPods and other media players, podcasts on important health-related issues are needed. Podcasts are audio files that can be downloaded from the Internet, stored on personal computers, and transferred to media players.

YouTube Clip: Prostate Cancer Education and Screening

John Ureda, South Carolina Cancer Disparities Community Network

The South Carolina Cancer Disparities Community Network has taken notice of two trends: barber shops in the African-American communities are an important forum for discussion of issues of concern to community members, and YouTube is increasingly being used as a way to get people started talking about subjects like colorectal cancer. Dr. Ureda demonstrated a You-Tube video clip showing a discussion about colon cancer in a barber shop. The South Carolina Cancer Disparities Community Network plans to use this video as part of an educational program targeting barbers and beauticians.

Estudios Clinicos! A Redes en Accion & CIS Collaboration

Kip Gallion, University of Texas Health Science Center at San Antonio

Mr. Gallion screened several public service announcements (PSAs) developed through a collaboration between the *Redes en Accion* project and the Cancer Information Service (CIS). These were designed to encourage participation in clinical trials among Latinos, a population severely underrepresented in clinical research. Four 30-second PSAs were created to stress the fact that enrolling in a clinical trial is a viable

option for Latino cancer patients. The airing of these PSAs has resulted in more than 550 telephone calls to CIS for further information. Six additional PSAs are under development.

The project has encountered difficulty in getting the attention of television stations because station staff often simply scan return addresses on envelopes and reject submissions because they are not familiar with the sender. The project has begun attaching images from PSAs to the outside of each envelope to illustrate the importance of the PSA's message.

Cancer Disparities in the Lives of Survivors and Their Loved Ones

Victor Tofaeono, LBJ Tropical Medical Center, American Samoa

Health disparities are a critical problem in American Samoa, where half the population lives below the poverty line. Before the CNP was launched in American Samoa in 2003, there had been no attempt to initiate a cancer control program in the area. Dr. Tofaeono is the only physician in American Samoa who sees patients with breast cancer. Mammograms (provided through a CDC program) must be sent to Hawaii for interpretation.

Because less than half the population of American Samoa has Internet access, the project relies on traditional media. Dr. Tofaeono demonstrated several video clips developed for television broadcast.

Key Points of Discussion—Session II-5

- v The Pew Charitable Trust and Kaiser Foundation have conducted surveys to capture information on how various age groups obtain information through traditional and new media. Participants should contact those organizations for information on their findings.
- v Video intended for dissemination through podcasts or YouTube does not have to be broadcast quality. Projects should take portable video cameras into community sites to capture real people in real situations. There are many sources of free software for disseminating video.
- v Different dissemination strategies may be appropriate for different settings (e.g., youth-oriented social networks versus faith-based organizations).

Concurrent Session II-6: Cancer Health Disparities—Epidemiology and Risk Factors

Moderator: Brenda Edwards, DCCPS, NCI

Study Dispels Low Cancer Risk Among Asian Americans

Beverly Gor, University of Texas M. D. Anderson Cancer Center

Most current literature indicates that Asian Americans have a lower general cancer rate but higher rates of cervical, stomach, and liver cancers than the rest of the population. However, the groupings for “whites” and “others” frequently include Asian Americans, and this masks the true incidence of health problems within Asian subgroups. Thus, the researchers conducted a health assessment to establish a disaggregated set of baseline data for use with future studies on Asian American populations. Additionally, the study aimed to compare data found in Asian American populations in Houston, Texas, with findings for other ethnic groups, and to provide the target communities with the data so that they can apply for community development funding.

Participants were Chinese and Vietnamese households randomly selected from a list of Asian surnames. The study chose those who were 18 years or older to take the Texas Community Health Survey, which had been translated into Vietnamese and Chinese and subsequently reviewed by the Asian Community Health Review Panel. After calling 4097 phone numbers over a nine-week period, the surveyors had

received answers from 1085 people; 814 of them completed the survey. About half were Chinese and half were Vietnamese, and nearly all of them were foreign-born.

The study found that Asians living in Houston were at-risk for cancer due to their lifestyles. Overall, they did not get adequate physical activity and did not eat enough fruits and vegetables (92.9 percent of the Vietnamese and 51.8 percent of the Chinese surveyed had not eaten 5 servings the day before the survey). They also had rates of obesity that increased with the amount of time that they had lived in the United States, low cancer screening rates (particularly for colorectal cancer), and a high percentage of Asian males were smokers. The next steps for this research include further analysis and dissemination of the data, developing culturally relevant cancer prevention education programs, improving the Asian Americans' access to healthcare, and performing a periodic re-surveying of the population.

Hispanic Health in Nashville 2007: Participatory Needs and Assets Assessment

Pamela Hull, Tennessee State University

The Hispanic population in Tennessee is over seven times bigger than it was in 1990. This initiative works with United Nashville Partners Against Cancer to gather data on cancer and general health needs within the Hispanic community in Tennessee.

The study developed a brief questionnaire, trained 15 Hispanic community members as interviewers, and then chose 500 local Hispanic adults as subjects. The sample characteristics turned out to be very similar to the data obtained by the 2000 census. The Hispanic population in Nashville was mainly composed of younger individuals and reflected a lack of education. Only 1 in 5 of the individuals surveyed had health insurance, and cancer was a main health concern, due to the fact that treatments are expensive and people diagnosed with cancer rely heavily on insurance. Also, a significant number of people surveyed said that they would have their daughters vaccinated for human papillomavirus (HPV) if the vaccine were free. In conclusion, this study shows that CBPR within the Hispanic community in Nashville is feasible, and that this can guide new community initiatives.

Use of Geographic Information Systems (GIS) and Asset Mapping to Illuminate Cancer Health Disparities in the Tampa Bay Community Cancer Network

Clement Gwede, H. Lee Moffitt Cancer Center and Research Institute

Asset mapping is the process of cataloguing the resources of a community. This creates awareness of local resources and information, identifies community strengths and uses resources to meet community needs, and simply recognizes and values the resources within a community. Asset maps are made with data from both individuals and the community. Resources that are mapped can include individual people, skills, and populations; social clubs, community events, and political campaigns; structured organizations, such as hospitals and schools, and the assets of these institutions; and economic assets. These lists of resources are mapped using Geographic Information Systems, which integrate the nonspatial information within spatial and geographic data. This way, users can assess local sociodemographic characteristics, supplies of resources, coordinate resources, and look at relationships between resources and users. Further, the data can be used to generate maps that are easy to understand and can be used for advocacy purposes.

For example, this tool can be used to locate community partners and analyze how they relate with an actual population. Another community partner assessment looked at the access to cancer-related services, finding that increasing access to cancer resources was a high priority, and that more people were aware of breast cancer needs than colorectal cancer needs. Thus, it developed a colorectal cancer screening and information guide as a starting point. Data can be viewed in a number of ways, including stacked columns and maps.

In the future, asset mapping can be used to map colonoscopies by funding categories in order to identify the best referral pathways for underinsured populations, to elucidate racial and ethnic disparities in cancer by mapping incidence and mortality data by race, and to increase the awareness of resources that are available to help with referrals. However, lack of resources, both for funding services and obtaining data, is a complication of asset mapping.

Pattern of Cancer Incidence Among U.S. Pacific Islander Patients: Evidence From the Surveillance, Epidemiology, and End Results Database, 1990–2004

Sela Panapasa, University of Michigan

The objectives of this CNP Pilot study were to establish disaggregated baseline data on the incidence of cancer among native Hawaiians and other Pacific Islanders and develop evidence regarding cancer disparities among these populations in order to inform new policies and intervention programs. Data for the study came from the US Census in 1990 and 2000, the Surveillance, Epidemiology, and End Results (SEER) database (1990-2000), and the mortality and fertility detail files. Then, the study conducted intercensal estimates, constructed a life-table, calculated age-specific cancer incidents, and calculated crude cancer incidence rates.

A special tabulation extracted native Hawaiians from Asian/Pacific Islanders. Prior to 1990, the US census included them all in the same category. In 2000, the data were available, but the definitions of the populations were different (people self identified as “native Hawaiian alone” or “native Hawaiian with another ethnic group”), so the study decided to use the 1990 definitions for race. Raw mortality numbers showed that younger native Hawaiians have a higher mortality rate, regardless of cause. Then, the study used SEER to calculate the crude rate of cancer incidence in whites, blacks, others, and Hawaiians according to the definition used by the 1990 census, finding that the Hawaiian subgroup had a much higher incidence of cancer than whites, blacks or the “other” category.

In summary, the study found that SEER data were a valuable resource for calculating baseline information on cancer incidence among native Hawaiians and Pacific Islanders. Without an accurate estimate on small populations, such as the ones featured in this study, it is impossible to understand their true risk of cancer. Future studies will require information on more specific population groups (subgroups of Pacific Islanders such as Fijians and Tongans) and will need to validate and test the methods used here. Bi-racial categories present a specific difficulty in analysis of demographics and epidemiology. Finally, the study must be used to help adopt specific policies to address the increased risk of cancer among these populations.

Data for Addressing Cancer Disparities in Arizona's American Indian Community

Zeenat Mahal, Inter Tribal Council of Arizona and Kathryn Coe, University of Arizona

Approximately 5 percent of the population in Arizona is Native American. Compared to other groups, Native Americans have a low incidence of colorectal cancer, but their survival rate after five years is poor. Late diagnosis and the lack of access to good care might be part of the reason for this problem, along with the lack of funding for these services. The Southwest American Indian Collaborative Network (SAICN) aims to reduce cancer disparities by providing more resources that can be used for cancer treatment and prevention to tribal communities. Part of this effort involves the Data and Evaluation Core, which promotes CBPR in Southwestern American Indian communities.

A matrix was developed to present scientifically sound options, their costs, and their benefits to tribal health decision makers. This empowers tribes by providing them with a guidance document that prioritizes actions likely to reduce the burden of cancer on their communities as well as a planning tool to help them take the lead in community interventions. Additionally, a matrix provides continuous updates on the types of cancer present in the tribes. The matrix was begun in 2006 and is based on extensive

research on cancer prevention strategies. The team researched the effectiveness, costs, and benefits of all of these strategies and compiled cancer burden and cancer screening data from the Arizona Cancer Registry, the New Mexico Tumor Registry, and the Indian Health Service. An SAICN Data and Evaluation Core advisory board was then consulted to add any updates that they felt were necessary. Additionally, there is space in the matrix for tribes to add new ideas.

The matrix has allowed the group to conclude that current cancer control efforts are getting the correct emphasis. They can also initiate cancer control programs, prioritize them, and recognize areas where more research is needed, just by looking at the information contained in the matrix. Next, the group's goal is to train the tribal leaders to use and modify the matrix by developing a workshop, a toolkit, an implementation plan, and by providing technical assistance to health planners and decision makers.

Tuesday, July 15, 2008

Plenary III—Eliminating Cancer Health Disparities: Communities Moving From Determinants to Solutions

Moderator: Leslie C. Cooper, Disparities Research Branch, CRCHD

Cancer Health Disparities: Research Leading to Elimination

Edward Partridge, UAB Comprehensive Cancer Center

There is a critical “disconnect” between discovery and delivery that contributes to the unequal burden of cancer. Many determinants, ranging from individual risk factors to social and economic policies, influence this disconnect. The aim of the UAB Cancer Control and Population Science program is to eliminate this disconnect and the resulting cancer disparities.

The UAB Cancer Control and Population Sciences program has grown from receiving approximately \$1 million in annual direct funding in 1992 to \$12.5 million in 2008. Early on, the program decided to address cancer health disparities in two areas of the region it served: (1) the Black Belt of Alabama, and (2) the Mississippi Delta. Initially, 10 women were trained to be community health advisors in a housing project; although the effort had little formal funding, it was successful, in part because it focused on service, not research. The UAB program partnered with a number of other programs interested in health disparities to form the Alabama Partnership for Cancer Control in the Underserved.

With funding from the Special Populations Network (now the Community Networks Program), UAB established the Deep South Network for Cancer Control and trained 800 community health advisors. The funding from this first successful grant application was leveraged to build the infrastructure of the program that exists today. Shortly thereafter, a REACH 2010 grant was obtained, which supported training an additional 250 community health advisors. The REACH funding transitioned to support for a Center of Excellence to Eliminate Disparities, which has expanded the service area of the program to six Deep South states. A Project EXPORT grant has also been obtained and partnerships formed with the Morehouse School of Medicine and Tuskegee University.

The UAB program eventually trained its community health advisors to carry out community-based navigation. This effort has been very successful: in the counties served by CNP, mammogram disparities of the Medicare population have decreased from 17 to 6 percent.

Lastly, that the UAB Minority Health and Research Center was established. This university-wide Center focuses on health disparities with the goals of building trust, sharing power, and eliminating racial bias. The research component of the Center consists is supported by approximately \$50 million in annual direct funding for health disparities research. The Center is also involved in training and community outreach.

Arkansas Colorectal Cancer Control and Research Program (Promoting Colorectal Cancer Screening in Primary Care Practices)

Ronda Henry-Tillman, UAMS/Winthrop P. Rockefeller Cancer Institute

Arkansas, especially the Arkansas Delta area, has one of the highest rates of colorectal cancer mortality. The Arkansas Delta has a large population of African Americans and low-income and low-education individuals, and has limited access to resources. In this area, the majority of colorectal cancer patients present with stage III disease. The Colorectal Cancer Control and Research Program stemmed from work of the Arkansas Special Population Access project, which studied awareness, education, and problems within the state regarding resources.

Data obtained from the Arkansas Community Cancer Education and Awareness Program revealed that both screening rates and resources were low, with significant regional differences. However, the program believed that this could be improved by providing interventions and strategies to promote screening in both primary care clinics and other settings. After 4 years during which the program provided evidence-based data to legislators, the Colorectal Cancer Act was finally passed in Arkansas in February 2005. The Act mandated insurance reimbursement for colorectal cancer screening; defined guidelines for screening; and established a 2-year Colorectal Cancer Control Program to obtain evidence-based data to support the statewide program.

It was discovered that only 50 percent of the state's population of over 2 million people had been screened according to American Cancer Society guidelines; the central and northwest regions of the state had the highest screening rates. This information prompted the setting of a goal to increase screening from 50 to 75 percent among disparate populations. Obtaining this screening goal would require an additional 225,000 screenings. The Colorectal Screening and Demonstration Research Project determined that reaching this goal could potentially result in a 2.5 percent reduction of cancer progression.

Arkansas is able to accommodate a statewide program to meet the ACS's screening goal of 75 percent with current medical personnel and facilities. Increased screening translates into prevention of cancer and a potential reduction in health care costs for colorectal cancer.

Power of Science, Culture, and Literacy in Generating Knowledge and Influencing Behavior: Toward a Better Understanding of Cancer Health Disparities

Cathy Meade, H. Lee Moffitt Cancer Center & Research Institute

Culture and literacy issues cut across the continuum of cancer care. Health literacy must be understood within the context of culture and language. Critical information gaps and training needs must be remedied in order to provide meaningful and understandable information that fits particular racial/ethnic communities. The biennial Cancer Culture and Literacy Conference seeks to address these concerns by discussing, developing, and testing a variety of methods that will improve health communications.

The Conference brings individuals together for networking; information learned can be applied back to one's community through research, education, or clinical practice. A variety of disciplines participate in these conferences, including: public health, anthropology, adult education, literacy specialists, and community partners. Conferences promote the application of knowledge and promising practices for interdisciplinary participants and enhance collaborations with other organizations and community members.

The Cancer Culture and Literacy Conference is a novel forum for the exchange of health literacy information that emphasizes the importance of placing disease and health experiences within a cultural, historical, and social context. Continued success of the conference depends on overcoming several challenges. Training and education are needed to meet the needs of diverse audiences (e.g., community and academic partners) and ongoing financial support is required to support the program. Also, systems need to be developed to facilitate wider dissemination of information and transfer of the current model to other settings. The next Cancer Culture and Literacy Conference will be held on May 20-22, 2010.

Navajo Language Translations of Cancer Terminology and Concepts

Martha A. Austin-Garrison, Diné College

Ms. Austin-Garrison worked with health educators from the Indian Health Service and the Navajo Nation Health Educators to develop a glossary of cancer terminology and concepts. Prior to this project, a specific word for cancer did not exist in the Navajo language. The terminology being used consisted of century-old words with negative connotations. It is difficult to treat cancer when patients are embraced with fear and have no hope for survival.

After the first task of creating a new Navajo word for cancer, all of the terms from the Portland Indian Health Board's Cancer 101 Project were translated into the Navajo language. The guide, which is similar to a dictionary, is culturally sensitive and intended for use by clinics, physicians, patients, the Navajo Nation community, and students.

ATECAR—Asian Community Cancer Network: Sharing Common Goals to Reduce Cancer Disparities in Underserved Asian Communities

Grace Ma, Temple University

Asian populations have the lowest cancer screening rates compared with all other racial/ethnic groups and are also one of the fastest growing populations in the United States. Certain cancers are more prevalent in Asian populations (e.g., liver and stomach), and there is an overall lack of subgroup cancer data at the national and local levels. The barriers Asian Americans face toward screening and care include high numbers of underinsured and uninsured, limited English proficiency, unfamiliarity with the health care system, limited access to health care, and lack of knowledge about their rights to care and screening. Asians experience the lowest satisfaction with screening and access to cancer care, and non-English speaking Asians experience the most difficulty in communicating with health care providers. The Asian Tobacco Education and Cancer Awareness Research Initiative (ATECAR) Asian Community Cancer Network was established to address these concerns.

The Network covers the geographic areas of Pennsylvania, New Jersey, New York City, Delaware, and parts of the DC area. The primary aim is to reduce cancer health disparities among underserved Asian populations through community-based participatory education, research, and training. The five major components of the Network are infrastructure building, community education, research focusing on behavior and clinical interventions, training, and dissemination. The Network has over 100 community-based organization partners, over 30 research and training institution partners, and over 35 clinical partners, providing a strong foundation for the aims of the program.

In terms of research, the Network has conducted a regional needs assessment, identified the determinants of the population, and developed pilot studies of 1 to 2 years to test feasibility. Data from the pilot studies were used to create research interventions for further testing of effectiveness. Intervention components include education, outreach, access to health care, diagnostic testing, and navigation for screening and treatment.

To illustrate the effectiveness of community-based participatory research programs, the results from a hepatitis-B pilot study were shared. There was a 30 percent increase in the ever-screening rate from baseline to 6-month follow-up; and there was an increase of 86 percent vaccination from baseline to 6-month follow-up. Findings from these pilot studies provided preliminary data for the program's NIH-funded R01 randomized trials. So far, the ATECAR Asian Community Cancer Network has been successful; in order to sustain such programs, collaboration among the clinical community and research partners must be strengthened and expanded.

Key Points of Discussion—Plenary III

- v Researchers should be sensitive to the fact that science has demonstrated that race is not a proper descriptive of biological differences in humans. Using the term “race” when trying to dissect the biology of health disparities only complicates the matter. However, as long as grantees received funding from NIH, they must use racial categories to report their data.
- v With the new Navajo cancer terminology, more Navajo Nation patients are asking questions about their bodies. Communicating in the Navajo language facilitates the cancer education process for these patients.

- v When working with Asian populations, it is necessary to tailor programs toward each subpopulation (e.g., Korean, Japanese, Vietnamese, Chinese) and culturally adapt concepts and education styles.

Plenary IV—Program Monitoring and Evaluation: Importance of National Evaluation and Local (Site-Specific) Data

Moderator: Emmanuel A. Taylor, Disparities Research Branch, CRCHD

The purpose of this panel is to inform the audience about the increased emphasis on program monitoring and evaluation within the Center to Reduce Cancer Health Disparities. An additional goal is to present examples of grantees making headway in reducing cancer disparities. The aim of evaluation is to ensure that specific policies are achieving what they are intended to achieve. The evaluation of local programs is especially important because they inform the evaluation of the overall national program, which funds a number of projects. Showing that a program has been successful and is well designed is key for obtaining continued funding. Local programs must provide timely and accurate data, so the Center can show the government and public that accurate and helpful results are being obtained.

Evaluating the Impact of Increasing Mammography Capacity on Screening Rates Among Low-SES Women in Lawrence, Massachusetts

Howard Koh, Dana-Farber Harvard Cancer Center

As the Principal Investigator of Massachusetts Community Networks to Eliminate Cancer Disparities through Education, Research, and Training (MassCONNECT), Dr. Koh has specific experience with community-based research. MassCONNECT has been in existence for 4 years. One of its main goals is to present information in a form that is understandable by everyone. For example, a map of Boston that is color-coded to show wealth distribution can be superimposed onto a map showing cancer disparities to demonstrate a specific trend. MassCONNECT works very closely with community coalitions within Massachusetts, with a specific focus on tobacco control, cancer screening (particularly mammography), and access to health care coverage. MassCONNECT also works with state government to reduce health disparities and to educate the public regarding progress made in state policies so that everyone can take advantage of those changes. Massachusetts is the only U.S. state to mandate health insurance coverage for individuals, with an additional mandate for employers to provide health insurance if they have 11 or more full-time employees.

MassCONNECT recently performed an evaluation of CDC-funded programs aimed at increasing screening for cervical and breast cancer. Massachusetts set up an organization called The Women's Health Network, which has provided screening services to 55,000 women over the past 10 years. MassCONNECT hopes to publish several articles that analyze the results of these screenings, including an analysis of whether women who had abnormal mammograms resolved those issues and how long it took to do so. In 2003, the median time between mammogram and diagnostic procedure had decreased to 0 days from an average of 86 days in 1998. Furthermore, the number of women receiving mammography at the recommended time intervals increased 18 percent after the establishment of a mammography center at the Greater Lawrence Family Health Center. Additionally, a mammography van based in Boston has begun rounds in Lawrence, Massachusetts, and has already provided service to approximately 180 women.

The Massachusetts State Health Department has also undertaken a project called Ready, Set, Quit, the goal of which is to decrease smoking rates. The project involves an intense 6-week outreach campaign. The state decided to focus on Worcester and Lawrence, two cities MassCONNECT focuses on as well. The campaign encourages smokers to call a quit line, provides them with nicotine replacement therapy, and monitors them over a period of time to assess quit rates. Out of 2,500 smokers who called the quit line, 2,000 received free nicotine replacement therapy. Approximately 20 percent of smokers who participated in follow-up calls reported being smoke-free for at least 30 days. Another ongoing project being

performed by the School of Public Health analyzes the targets of tobacco advertising campaigns, hypothesizing that these campaigns are directed at minority groups and those with lower socioeconomic status.

How AANCART Addresses Challenges in Evaluating the Reduction of Cancer Health Disparities Among Asian Americans

Moon Chen, University of California, Davis Cancer Center

The Asian American Network for Cancer Awareness, Research, and Training (AANCART) is currently evaluating cancer health disparities in Asian Americans. The organization has found that cancer is the leading cause of death for this population and that Asian Americans are the only U.S. population for which cancer is the leading cause of death. Limitations for studies conducted by this group include lack of resources, lack of locally specific baseline data, and cultural/linguistic diversity. Asian Americans are an incredibly diverse group of people, as they originate from a variety of places. To deal with these issues, AANCART focused its studies on four specific city populations and chose one cancer disparity for each population. The organization focuses on the Cambodian population in Seattle, the Vietnamese and Chinese populations in San Francisco, the Korean population in Los Angeles, the Filipino population in Hawaii, and the Hmong population in Sacramento.

One example of a completed project focused on colorectal cancer among Vietnamese in San Francisco. The dissemination of a culturally specific brochure, along with telephone counseling and follow-up interviews, yielded a statistically significant increase in screening among that population. AANCART has also increased the availability of mammogram services in Hawaii, as well as colorectal screenings in Los Angeles. In Hawaii, the group found that it had more success in working directly with Filipino women's groups, as opposed to working with physicians. For the San Francisco Chinese population, AANCART focused on increasing the public awareness of screening guidelines, which resulted in a 10-percent increase in the number of colonoscopies. In Sacramento, the focus was on the Hmong population, which has no word for cancer; thus, the group had to educate that population on a basic level. Currently, there is a Hmong radio talk show in the area dedicated to addressing cancer.

Over time, AANCART has built its capacity for research and analysis. For example, it has developed a study of Hepatitis B knowledge among Cambodians that has also been applied to efforts to increase screening for Hepatitis B in Hmong, Vietnamese, and Korean populations simultaneously. Additionally, it functions as an interface between the scientific research community and the general population and has seen considerable, measurable impact of its efforts on the availability of cancer screening.

Key Points of Discussion—Plenary IV

- v Currently the National Cancer Institute focuses only on ethnic, rural, and underserved populations, per the definition of “health disparities” provided by the NIH. Thus far, this definition does not extend to lesbian, gay, bisexual, and transgender populations, though they may be included in an ethnic or underserved population.

Concurrent Session III-1: Emerging Technology Applications

Moderator: Jerry Lee, Office of Technology and Industrial Relations, NCI

Development of Degradable Stealth Nanospheres for Controlled Delivery of Anticancer Drugs

Emmanuel Akala, Department of Pharmaceutical Sciences, School of Pharmacy, Howard University

New approaches to drug delivery are based on the idea that the best biological response will be achieved with optimal spatial placement and temporal delivery of bioactive agents. In addition to advances in drug

delivery systems, there have been developments in the formulations of materials; the advent of biodegradable and biocompatible polymers has increased the versatility of these materials. Polymers have been used as components of many drug delivery systems such as targetable, modulated, and self-regulated nanoparticles and gene delivery systems.

The ultimate goal of the current project is to develop multifunctional nanoparticles for cancer chemotherapy. To date, biodegradable stealth paclitaxel-loaded nanospheres have been developed that passively target tumors due to enhanced permeability and retention effects. The results of statistical experiments show that the size of these nanospheres depends on the concentrations of the cross linker and monomer. Scanning electron micrographs reveal that the nanoparticles are spherical with smooth surfaces. Transmission electron micrographs give evidence of a cross-linked core with a polyethyleneglycol corona (shell). These nanospheres will be tested in cell lines and in animal models.

Future plans include targeting nanoparticles to receptors or other antigens on cancer cells. Also of interest is developing a combination therapy approach that involves use of RNAi to inactivate genes that promote tumor growth.

Statistical Analysis of Hematoxylin and Eosin Stained Nuclei from Breast Cancer Tissue

Manuel Ruidiaz, University of California, San Diego Moores Cancer Center

A system is needed to quickly help differentiate normal and cancer cells. Tissue sections allow for definitive evaluation of pathology, but these types of analyses are time-consuming and somewhat subjective. A semi-automated system for statistical evaluation of histological sections of breast cancer has been developed. Pathologists examined 30 hematoxylin and eosin (H&E)-stained tissue sections and classified them as high- or low-grade ductal carcinoma *in situ*, high- or low-grade invasive, or benign. Automated feature extraction was then used to identify single cell and novel group characteristics that could differentiate normal and cancer cells. Single cell characteristics included shape and size parameters (e.g., area, perimeter), pixel intensity, and cell positions. Novel group characteristics included local nuclear density, distance to nearest neighbor, ratio of nuclear area to neighborhood area, number of nuclei, and architecture. These criteria were used to evaluate surgical pathology samples.

Linear discriminant analysis (LDA) revealed that automated analysis could distinguish between benign and low-grade invasive cells with 99 percent certainty. This study shows that identification of different types of breast cancer can be accomplished using H&E-based image analysis. Single cell parameters also allowed separation of normal and ductal carcinoma *in situ* cells. Inclusion of neighborhood parameters provided even better separation of different cell populations. Automated discrimination analysis provides fast, accurate, quantitative, and objective data. In the future, this type of process will improve quantitative pathological analysis of challenging specimens, such as fine needle aspirations, in clinical settings. Work is also being done to develop nanoparticle libraries to assist with cancer identification.

Optimal Binding Interactions on Adhesive for Selective Capture of Breast Cancer Cells From Human Tissue

Sergio Sandoval, University of California, San Diego

Approximately 192,200 women in the United States are diagnosed with cancer every year. Breast conservation therapy is the primary treatment option for early stages of breast cancer; however, 20-40 percent of these patients will need to undergo a second surgery because the tissue removed has positive margins (i.e., there are still cancer cells at the edges of the removed tissue, meaning that tumor cells were likely left behind). This is not discovered until after the surgery when the removed tissue is evaluated. Second surgeries are not only expensive, but can be emotionally difficult for the patient. The goal of the

current project is to develop an automated system that *intraoperatively* analyzes the margins of the removed tumor.

To develop such an approach, touch preps were done on excised surgical tissue using poly-L-lysine coated slides. Poly-L-lysine was chosen as a coating because it binds cells through electrostatic interactions instead of covalent bonding. These samples were then subjected to a rapid immunofluorescence protocol through which they are stained for an epithelial cell marker and with a nuclear stain. Breast cancer cells were identified using both automated and manual analysis and the results of these two approaches compared. The results of manual and automated microscopy were similar. Automated microscopy was able to detect positive margins for both invasive ductal and lobular carcinomas; however, the data were insufficient to determine if the approach worked for ductal carcinoma *in situ*. Other approaches may be needed to detect this type of lesion.

Key Points of Discussion—Session III-1

- v Intellectual property issues should be resolved when collaborative relationships are initiated. This issue must be addressed to promote the formation of multidisciplinary teams to address urgent clinical needs.

Concurrent Session III-2: Clinical Factors Involved in Diagnostic Delay

Moderator: Jo Anne Zujewski, Division of Cancer Treatment and Diagnosis, NCI

Missed Diagnoses: Factors Associated With Inaccurate Digital Rectal Exams

Carla Pugh, Northwestern University

The clinical digital rectal examination (DRE) is an important part of colorectal and prostate cancer screening. The DRE simulator uses mannequin-based models to evaluate examiners. Sensors are placed in the “task trainer” models, which allow detection of where the examiner is touching and how much pressure is being applied. A study was designed to test the hypothesis that the simulator would be able to detect quantifiable differences in DRE technique between students and experienced urologists. Participants included 200 third-year medical students and 420 urologists. Two task trainers were used—the first had a normal rectum and a 2 cm nodule on the right lateral prostate lobe and the second had an irregular 5 cm rectal mass and benign prostatic hypertrophy. Upon completion of the DRE, all participants were asked to document their findings on a standardized clinical assessment form, and computer-generated quantitative performance data were collected from the task trainer models. Medical students spent less time on the exam than experienced urologists and palpated fewer areas. Students were less accurate in their assessment of the prostate, but were actually more accurate than the urologists in their assessment of the rectum of the second task trainer. Factors affecting student accuracy were largely related to lack of palpation proficiency—many students focused on pronating and supinating rather than lateral palpation. Many of the urologists did not perform complete DREs; in fact, half failed to examine the rectum. Additional data will be collected from students and colorectal surgeons. It will be interesting to determine whether colorectal surgeons administer DREs differently than urologists.

Influence of Gender and Race on Diagnostic Delay in Colon Cancer

Laura Siminoff, Virginia Commonwealth University

Compared with their white counterparts, African Americans have higher incidence rates of many cancers, including colorectal cancer. African Americans are also more likely than whites to be diagnosed with colorectal, lung, breast, cervical, and prostate cancers at advanced stages, and are 34 percent more likely to die of cancer than whites. “Appraisal delay” refers to patient delays in seeking medical care or advice;

appraisal delay is influenced by difficulties with symptom identification, inaccurate symptom interpretation and/or attribution, and psychosocial factors. Appraisal delays can result in diagnostic delay, but diagnostic delays can also result from structural barriers to healthcare access and ineffective patient-physician communication. Gender and cultural factors may also influence these processes and account for some of the observed disparities.

The objective of the current study is to examine the influence of gender and race on diagnostic delay using qualitative methods. Patients diagnosed with colon cancer in the past 2 years at Virginia Commonwealth University's Massey Cancer Center in Richmond, Virginia, and the Case Western Reserve University Comprehensive Cancer Center in Cleveland, Ohio, are recruited and interviewed over the phone or in person. The semi-structured patient interviews are organized into six parts: (1) symptom recognition and appraisal; (2) influence of family members and friends; (3) social support; (4) ease of access to care; (5) communication with health care providers; and (6) sociodemographic and psychological factors. To date, 14 patients have been interviewed. The median time between patient diagnosis and interview was 5 months. Overall, the patients claim to clearly remember the events leading to their diagnosis and provided detailed descriptions of their symptoms without hesitation; however, they had more difficulty reconstructing conversations with their healthcare providers, which may be due in part to low levels of health literacy. The time between first visit to a medical provider and colorectal cancer diagnosis ranged from 0 to 13 months. Shorter time to diagnosis correlated with more severe symptoms (i.e., symptoms that drove patients to go to the emergency room). In general, white patients did not wait as long as African American patients to seek care.

The second part of the study will be a simulated patient experiment that measures the effects of patient characteristics on physician behavior. One hundred ten primary care physicians (half male, half female) from community practice-based research networks will see four different patients with colorectal cancer—an African-American male, an African-American female, a white male, and a white female. Patient interactions will be recorded and coded. The physicians will not know when they are interacting with one of the simulated patients. This component of the study will be informed by the results of the patient interviews.

Time to Resolution Following Abnormal Mammogram for Low-Income, Uninsured, or Underinsured Women

Rebecca Lobb, Harvard University School of Public Health

Diagnostic and treatment delays can lead to a more advanced stage at diagnosis and poorer survival. Compared with white women, black and Hispanic women experience longer times to diagnosis and treatment. These disparities are often explained by insurance status, income, education level, and patient/provider communication.

The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was created in 1990 to remove barriers to early detection of breast cancer for low-income, uninsured, and underinsured women. It provides free screening and cancer detection services to women across the United States. Since 1998, the program has provided case managers and patient navigators to improve appointment keeping, increase completion of diagnostic resolution, and reduce time to diagnostic resolution after an abnormal mammogram. The objective of the current study is to investigate whether women who received breast cancer screening services through the NBCCEDP in Massachusetts obtained diagnostic resolution for an abnormal mammogram within 60 days. Data were obtained from the Women's Health Network on NBCCEDP participants who had had an abnormal mammogram (BI-RAD 04, 05). Information on all diagnostic procedures (e.g., biopsies, diagnostic ultrasounds) and diagnostic resolution (i.e., cancer confirmed or ruled out) were included as was patient demographic information such as age, race, primary language, and education.

Using unadjusted survival analysis, the median time to first diagnostic procedure and diagnostic resolution following an abnormal mammogram were measured. A subset analysis was also performed on women who had achieved diagnostic resolution to determine whether time to resolution varied with patient characteristics. Among 2,876 women, median time to first diagnostic procedure was 8 days, and median time to diagnostic resolution was 74 days. Median time to first diagnostic procedure decreased from 23 days (1999) to 0 (2003), and remained at 0 days throughout 2007. The proportion of women whose diagnosis was resolved within the program standard (60 days) was 42 percent in 1999 and increased to 64 percent in 2007. Improvements in time to first diagnostic procedure corresponded with the initiation of targeted funding for patient navigators in 2001. Timely resolution after an abnormal mammogram is influenced by patient, provider, and health center characteristics; however, there were no significant differences in time to diagnostic resolution between racial/ethnic groups.

Next steps will include analyzing data from earlier years to examine trends in time to resolution prior to 1998. Survival analysis will also be used to examine bivariate and adjusted associations between covariates and outcomes. Variability in time to event will be assessed across medical service sites to understand sources of variation and best practices. Other policy, practice, and patient factors that may explain improvements in time to resolution for Women's Health Network clients will also be pursued.

In Due Time: Women's Accounts of Their Protracted Responses When Told to Follow Up on Suspicious Pap Test Results

Karen Freund, Boston University Medical Center

Ethnic and racial minorities often experience diagnostic delays. Some factors contributing to this are lack of economic resources, competing demands, logistics, and health literacy. Women respond to suspicious test results in their own meaningful ways; however, understanding of women's perspectives remains limited. The current study used open-ended interviews to explore women's own explanations for delaying follow-up following an abnormal test result. Women who had received an abnormal Pap result after being screened at a Boston community health center were initially identified by chart review. Of the 80 women identified, 14 participated in the study (3 attended a focus group and 11 were interviewed by phone). Of the 14, 7 were African American, 4 were Caribbean, 2 were Hispanic, and 1 was Native American. The median age of the participants was 24 years.

Some women reported being alarmed by their Pap results, but others accorded them little significance, citing histories of false positive test results. Many women were concerned about fertility or afraid of having cancer. For some, the result raised questions about marital fidelity, suggesting that physicians do not always explain to patients that an abnormal Pap result is not always related to sexual activity. Follow-up was also complicated for some adolescents because they did not want to admit to their parents that they were sexually active. Several patients expressed dissatisfaction with their providers, and many also cited lack of insurance or inability to take time off work as barriers. Some of the interviewees who lived in a shelter said that the shelter's schedule made it difficult for them to get follow-up care. In general, healthcare providers had a tendency to ignore or minimize the reasons for the delays.

An abnormal Pap result means different things to providers/researchers and patients. Providers and researchers view an abnormal result as a possible indication of cervical cancer that necessitates follow-up examination. However, for patients, an abnormal Pap result may evoke a wide range of emotions, which may vary depending on knowledge and prior experiences. Clinical follow-up is only one of the many demands that a patient must manage. Patient navigators serve as a bridge between these two perspectives. Navigators should take the patient's account at face value, at least initially, and spend time understanding the patient's frame of reference. They can then convey relevant information to healthcare providers. These findings highlight how the worldviews of vulnerable women influence their decision to obtain follow-up care for an abnormal Pap result. This information may help guide interventions to ensure equitable care.

Concurrent Session III-3: A Greater Understanding of Breast and Cervical Cancer in Minority and Disadvantaged Populations

Moderator: Barbara Terry-Koroma, U.S. Army Medical Research and Materiel Command

Impact of Interpreters on Breast and Cervical Cancer Care Services for Thai and Vietnamese Patients

Tu-Uyen Nguyen, California State University, Fullerton

Inadequate numbers of professionally trained interpreters and medical interpretation services are major barriers to cancer screening, diagnosis, and follow-up. Patients with limited English proficiency have fewer visits, receive fewer preventive services, are less likely to return for care, have longer hospital stays, know less about their health, and are more likely to receive inaccurate communication than those who understand English. A person is Limited English Proficient (LEP) if he or she responds “less than very well” to the U.S. census question, “How well do you speak English?” The Civil Rights Act requires state- and federally-funded health care facilities to provide translation services to LEP patients free of charge. A Professionally Trained Health Care Interpreter is someone who has been trained through a course, agency, or certification program; there is no federally mandated training or certification process. A medical interpreter must be proficient in both languages, familiar with medical terminology and ethical principles, and trained in interpersonal and communication skills.

Between 2002 and 2004, PALS for Health received over 80 calls from Thai women and over 50 calls from Vietnamese women related to mammographic health care. The PALS director wanted to know why so many of these women were asking for interpreters regarding breast and cervical health issues. The aim of this study was to identify the discrepancy between the perceived need for and the actual resources for interpretation services. The researchers will be conducting phone interviews with 50 Vietnamese women and 50 Thai women in Los Angeles. The goal is to recruit 25 women from each ethnic group who used trained interpreters and 25 from each ethnic group who had not requested them. Quantitative and qualitative questionnaires were developed for the interviews. To date, 85 of the 100 planned interviews have been completed.

Interview responses have so far indicated that people do not understand the difference between trained and untrained interpreters. Family members often serve as interpreters, although patients who have used trained interpreters report being more satisfied with their health care. One major consideration that determined whether people used trained interpreters was convenience. People wanted their interpreters to have both technical skills and interpersonal abilities. Due to the fact that there are more Vietnamese than Thai doctors in the Los Angeles area, researchers hypothesized that the Vietnamese population would not have as great a need for interpreters. However, this hypothesis was not supported by the findings, which indicated that the majority of the employees operating technical equipment (e.g., mammography equipment) do not speak Vietnamese even if the front desk employees are Vietnamese. For the most part, patients used interpreters for non-routine care more than for routine doctor’s visits. The only gender preference expressed was for female interpreters when dealing with cervical and breast cancer exams.

In summary, there is a great need for professionally trained interpreters whose services are free and convenient; however, patients do not always know when they have the right to request an interpreter. The next steps for the study are to complete interviews and data analysis and then disseminate findings. In the long term, the goal is to develop programs to promote use of interpretation services in Asian and Pacific Islander communities. Additionally, the program would like to consider conducting larger studies and explore the possibility of phone and video interpretation services.

Influence of Cultural Factors on Mammography Use Among American Indian Women

Angela Gonzales, Cornell University

Although breast cancer is the leading cause of death among American Indian women, the mammography rate among these women falls below the national average. It is important to understand whether the cultural importance of traditional Native American healing practices influences mammography screening.

The goal of this study is to estimate the lifetime rates of breast cancer screening on two Northern Plains reservations (Cheyenne River and Pine Ridge) and one Northwestern reservation (Gila River) and then determine whether cultural factors have an influence on mammography. The study surveyed 941 Native American women 41 years old or older, asking them to self-report mammographies. Women between the ages of 41 and 50 had the highest rate of mammography, and women over 70 had the lowest. The use of traditional practices to prevent illness varied between reservations. Women who received mammogram services were more likely to live close to a healthcare facility, be employed, and have more money and a higher level of education than those who did not. There were no associations between receipt of mammograms and the use of traditional medicine or cultural identification.

Thus, the researchers have concluded that traditional Native American healing practices and cultural identity do not play a role in determining whether women receive mammograms, and that traditional and modern medicine are coexisting in these populations. However, the study was limited by its reliance on self-reported data and the lack of information on insurance status and distances to healthcare clinics.

Assessing the Association Between Westernization and Lifestyle Factors, Reproductive Factors, and Breast Cancer Clinical and Histology Characteristics in a United States/Mexico Sample

Jesse Nodora, Arizona Cancer Center

Breast cancer in Latina populations is not well understood, though the profile of tumor presentation among Hispanic women is consistent with a more aggressive disease pattern. Additionally, cancer risk factors that are attributable to westernization are not well understood. As the U.S. Hispanic population grows, ages, and adopts American lifestyles, there is the potential for a major public health problem. Breast cancer mortality rates are also rising in Mexico; since 2006, breast cancer has become the leading cause of cancer-related deaths among Mexican women. Furthermore, data from Mexican women show an earlier onset of cancer than in whites. Because the Hispanic population is largely Mexican, as well as being underserved and underrepresented in clinical trials, it is important for the United States to partner with Mexican health initiatives.

The Binational Breast Cancer Study was undertaken to identify types of cancer most prevalent in women of Mexican descent, ascertain whether the pattern of disease changes in women who migrate from Mexico to the United States, and determine whether there are risk factors associated with certain types of breast cancer among Mexican women. Compared with non-Hispanic women, women of Mexican descent tend to be diagnosed with breast cancer at a younger age and present with larger, later-stage tumors. In a study published in the *New England Journal of Medicine*, Dr. Peggy Porter points out several facets of the western lifestyle that increase the risk of breast cancer, including diet changes, increased inactivity, later pregnancies, use of hormone-replacement therapy, reduced breastfeeding, and obesity.

The study aims were to develop and pilot a westernization questionnaire to assess the relationship among westernization, lifestyle, reproductive factors, and clinical aspects of breast cancer in Mexican and Mexican-American women. Additionally, the study sought to explore the association between Westernization and a specific tumor marker. The researchers hypothesized that Mexican women with greater Western influences would exhibit lifestyles and reproductive factors similar to American women, and also exhibit lifestyle, reproductive factors, and breast cancer characteristics similar to acculturated

Mexican-American women. To that end, the researchers have interviewed 200 Mexican women who have been diagnosed with breast cancer. Key measures of westernization include self-reported level of American influence, English-speaking abilities, American media and Internet consumption, American product consumption, an emphasis on individuality as opposed to family dynamics, level of materialism, ancestral identification, amount of time spent in the United States, and whether one lives in an urban or rural area. Because many cancer risk factors are lifestyle-related and thus preventable, a greater understanding of how these lifestyle factors relate to breast cancer characteristics could result in more successful prevention, screening, and diagnosis. Results from the interviews will inform further research and practice.

Knowledge and Attitudes About the HPV Vaccine in Appalachia Ohio

Mira Katz, The Ohio State University

The Appalachian region, which spans 410 counties and areas of 13 states, has high rates of poverty, disability, and unemployment and low levels of education. Cervical cancer rates in Appalachian Ohio are much higher than in other areas of Ohio (11.5 percent versus 8.3 percent). Cervical cancer mortality rates are similarly high: 3.9 percent in Appalachian Ohio and 2.7 percent in non-Appalachian Ohio. Only 79 percent of women in Appalachian Ohio have had a Pap smear in the past year, versus nearly 87 percent in non-Appalachian Ohio. The purpose of this study is to gain a better understanding of beliefs about and attitudes toward the HPV vaccine at both the individual and the community level in Appalachian Ohio.

The study developed a focus group guide based on the Social Determinants of Health framework. Focus groups were audiotaped and transcribed verbatim. Later, transcripts were reviewed and a coding tree developed. People from 14 different counties in all four regions of Ohio Appalachia participated in a total of 23 focus groups. The 114 participants included 27 women between the ages of 18 and 26, 19 parents, 37 healthcare providers, and 31 community leaders. One-third of the women and parents had less than high school education, and most of the participants were Caucasian. Questions on HPV knowledge were presented in true/false format. The researchers found a mixed level of acceptance for the vaccine between focus groups and even within groups. Participants displayed a lack of knowledge about HPV and how vaccines work. There was a lack of awareness about the vaccine and logistical details, such as where and when to get vaccinated, how many injections are needed, who should be vaccinated, and how much the vaccine costs. Healthcare providers and lay people alike were unsure whether the vaccine should be given to a woman who is already HPV positive. Participants also reflected the attitude that prevention is not a priority and that potential state mandates represented government intrusion into private lives. Findings showed that religious groups have a strong influence on the community. Participants also distrusted pharmaceutical companies, felt that healthcare providers did not respect them, viewed HPV as strictly a female problem, and thought that the vaccine would encourage risky sexual behavior. Similarly, participants thought that others would pass judgment on girls who received the vaccine. Other barriers to vaccination included lack of access to healthcare, cost and a lack of insurance, privacy concerns, fear of injection (site pain, weight gain, fainting), and fear of the vaccine itself (unknown long-term effects and potential effects on the reproductive system).

In the future, educational programs should be designed to provide comprehensive information to answer all of these questions. They should also provide information through trusted sources (i.e., not men in suits from the pharmaceutical company) and have women with personal experience with HPV and cervical cancer tell their stories. This information should also be available via the Internet.

African American Attitudes Toward HPV Vaccination

Vetta Sanders Thompson, Saint Louis University

The incidence of cervical cancer in African-American populations exceeds that of the general U.S. population. The mortality rate due to cervical cancer is also higher in African Americans than the rest of

the population. One factor in the development of cervical cancer is infection with HPV. African-American women have an HPV prevalence of 39.2 percent, and about half of these HPV infections are caused by the HPV16 virus. 19.1 percent of African-American women have HPV16, as opposed to 12.5 percent of white women. The new prophylactic HPV vaccine, which is effective against HPV16, is recommended for girls as young as nine, but primarily for girls who are 11 or 12 years old. Ethnic minority women have shown a general lack of knowledge and awareness of HPV (67.5 percent had never heard of HPV, compared with 58 percent of white women), and only 41.4 percent of African-American women believed that HPV is a cause of cervical cancer in 2005. Thus, not as many African Americans as whites are vaccinated.

This study aimed to (1) identify social and cultural factors that influence African-American parents' decisions to have their daughters vaccinated for HPV and (2) develop culturally relevant HPV vaccination promotion materials. The researchers conducted focus groups of 35 people and interviews of 10 people in the St. Louis metropolitan area. They found that African Americans have limited knowledge of cervical cancer. There was only a limited knowledge of HPV, and those aware of HPV were familiar because of personal experience or contact with someone who had the virus. Most participants had never heard of the HPV vaccine, and those who had heard of it had personal experience or had based their knowledge on television ads. Participants had mixed feelings about the vaccine, and were concerned about the cost and potential side effects. They were largely unaware of who should be vaccinated or of the fact that the vaccine's efficacy in older women is not yet known. The next step for the study is a cross-sectional survey of 200 parents of vaccine-eligible girls and 30 in-depth parent interviews. It is hoped that these will allow assessment of individual characteristics, cultural attitudes, and social and environmental factors that affect African-American parents' intent to vaccinate their children against HPV.

Concurrent Session III-4: Evidence-Based Intervention: Examples From the CIS Partnership Program's Body & Soul Dissemination

Moderator: Alexis Williams, Office of Communications and Education (OCE), NCI

Overview of the Body & Soul Program

Alexis Williams, OCE, NCI

The Body and Soul program is an evidence-based intervention aimed at reducing health disparities in African Americans. Delivered through African-American churches, it has proven to be effective at changing behaviors such as diet and level of physical activity. There are four pillars of the program: a commitment by the pastor to be involved; inclusion of church activities that promote healthy eating; a church environment that promotes healthy eating; and peer counseling that motivates church members to continue their healthy habits. The program was initially disseminated by ACS volunteers and staff members, through African-American media, and through a few African-American church denominations. Later, the program expanded to include dissemination through other community partners. The roles of community partners are to promote the program to churches, facilitate the adoption of the program, and provide technical assistance for the program. Community partners are not responsible for implementing the program for churches—implementation by the churches is essential for sustainability of the program at the church level. Body & Soul programs have been established in the continental United States and in Hawaii.

Body & Soul in Florida: Connecting Communities for a Healthier Lifestyle Through Partnership With the NCI Cancer Information Service

Cynthia Seaborn, Cancer Information Service, NCI

The Cancer Information Service is a national education and information network program. CIS is divided into 14 regions and has three main components: a partnership program that collaborates with organizations on the state and national level; an information service that provides individually tailored interactions; and a research program that fosters health communications and cancer control research. CIS is operated through contracts with academic institutions, cancer centers, and hospitals.

The CIS Partnership Program collaborates with selected organizations to provide information on cancer to underserved populations. This arm of CIS, with 70 employees nationwide, is responsible for disseminating NCI programs and materials, providing capacity-building expertise to organizations, linking organizations with similar goals, planning and evaluating programs, providing training on cancer-related topics, and providing research support. The Program addresses cancer health disparities by working with communities that suffer from an unequal burden of cancer, leveraging resources to address these disparities, and providing technical assistance and training to its partners. CIS concentrates on awareness and education, breast and cervical cancer, education about clinical trials, tobacco control, and cancer control planning. CIS has over 750 partners engaged in cancer control and education projects.

Body & Soul Plus: Engaging Researchers to Support the Dissemination of Body & Soul in Hawaii

Kevin Cassel, University of Hawaii Cancer Research Center

Currently, African Americans make up only 3 percent of the population in Hawaii and 1 percent of the population on neighboring islands. About 56 percent of the African Americans in Hawaii are affiliated with the military. There are only two African-American churches in Hawaii, though there are chaplains who serve the populations living on military bases. Since the 1980s, Hawaii's Five a Day Coalition has leveraged diet and nutrition resources, making it an attractive partner for CIS. CIS has also entered into a lucrative partnership with the Honolulu Black Nurses Association, which has been involved in community intervention research efforts and is an ideal partner for dissemination of the Body & Soul program. The program has also had great success implementing interventions with the cooperation of the U.S. Armed Forces, since all U.S. military branches are represented in Hawaii. Another source of cooperation is two doctors at the Cancer Research Center of Hawaii.

In order to gain information on how to encourage participation in the Body & Soul program, the group launched a research program to identify implementation issues faced by program partners and determine whether feedback affects participation. The researchers put a delayed intervention plan into place: during the first year subsequent to program kickoff, the intervention church will receive Body & Soul and extra Body & Soul Plus resources and the control church will receive standard Body & Soul resources. During the second year, the control church will receive the Body & Soul Plus resources. Participation rates for both churches will be measured for the first year of the intervention. Body & Soul Plus resources include a blood pressure cuff, a visual representation of one pound of fat, scales, and a pedometer for each participant.

At the Trinity Church program kickoff, nursing students performed biometric measurements to provide baseline data for the church. On the whole, values for the church were poor. The program then developed posters for the church to communicate these findings to the congregation. The researchers do not yet know whether this type of feedback will result in continued participation in the program. Potential problems include the limited number of churches to work with, the high percentage of military personnel among the African-American population (who are more likely to be physically fit compared that the non-military population), and limited resources with which to support the churches. The Body & Soul

program may also be adaptable to other populations in Hawaii that have strong bases in faith, similar dietary-related health risks, and large church followings (e.g., American Samoans). Next, the study will kick off a program at the Armed Forces Chaplaincy, identify mechanisms to provide feedback to participants, and find resources to support program implementation.

Adapting Body & Soul for Rural Communities

Gail Hardin, Cancer Information Service (CIS), NCI

NCI has organized a partnership with the African Methodist Episcopal Church on a national level. The organizers worked within the pre-existing church structure to provide training in the Body & Soul program, but also extended assistance to other community organizations such as the Tallahassee Memorial Hospital, which has offices throughout the region, and other organizations that have access to rural populations. Additionally, the group developed a flier-based campaign to publicize the free training programs. After volunteers receive training, they recruit more churches and run the next training; thus the program builds itself with CIS as a mentor.

Overall, churches are very happy with the programs; even smaller churches have found ways to adapt and implement the Body & Soul program. Barriers to success include difficulty obtaining access to rural communities and fear that participating in programs like Body & Soul will take up too much time. To address the latter concern, CIS developed newsletters, resource guides, and community guides to show that the time commitment is not prohibitive and to foster competition between groups.

Getting Body & Soul Into Your Community: Partnering With the Cancer Information Service

Evelyn Gonzalez, CIS, NCI

In the Bible Belt region of the United States, the church is the center of many people's lives, making the Body & Soul program particularly relevant. The Deep South Network covers 22 counties in Mississippi and Alabama. After polling key community leaders and advisors, researchers found that there was a high demand for information on nutrition, physical activity, and walking. This led organizers to choose the Body and Soul program. The network has trained 28 community leaders as partners. Additionally, these leaders have trained lay health advisors who work with the churches. The program is being implemented over the next 2 years.

Most of the churches being served are rural and have limited resources and space, so that programs like Body & Soul need to be implemented creatively. The Deep South Network for Cancer Control has thus far recruited 25 churches in the Mississippi delta to commit to the program. Eight of them have applied for a \$7,400 grant from the Fannie Lou Hamer Cancer Foundation. Each of these eight churches has chosen a church coordinator, set up a planning committee, and hosted a kick-off event.

The three most important barriers facing these programs are inadequate funds, demands on pastors' time, and difficulty getting members to complete the baseline survey for the Deep South Network for Cancer Control, which must be completed by 75 percent of the adult membership. NCI plays a significant role, but cannot offer money to help programs get off the ground. By the same token, it does not cost churches anything to work with NCI, and each church can adapt the program so that it best suits individual congregations.

Key Points of Discussion—Session III-4

- v Anyone capable of working with churches and mentoring is eligible to sponsor a Body & Soul program.
- v Conducting needs assessments of local church congregations will help identify churches that would be receptive to the Body & Soul program. Needs assessment results can also be helpful for convincing

pastors or others in church leadership positions that there is interest in the program. CIS is considering development of a needs assessment tool but there is currently no such tool available.

- v The National Black Leadership Initiative on Cancer III also has health programs and curricula that are adaptable for target populations. Community members and organizations interested in implementing programs within the community should determine whether programs that meet their needs have already been developed before spending resources to develop new programs.
- v Many people cite cost as a barrier to eating fruits and vegetables. They should be encouraged to eat appropriate portions and to select produce that is in season, both of which will reduce costs. Some churches have planted gardens and sell fruits and vegetables to the community at low prices.

Concurrent Session III-5: Innovative Research Methods

Moderator: Donald Dudley, University of Texas Health Science Center at San Antonio

Measuring What Navigators Do for Patients: Development of an Instrument to Assess Tasks and Use of Social Networks

Tracy A. Battaglia, Boston University School of Medicine

Patient navigation is a process of linking patients to complex cancer services, circumventing barriers, organizing services, and tracking patients through treatment. This process is emerging as a model to help reduce cancer health disparities experienced by low-income patients. Many navigation programs have been initiated, but wide variation in the roles of navigators in different programs has made it difficult to assess the contribution of specific components to optimal patient outcomes. The current project aims to develop a technique for observing a patient navigator's work to produce valid and reliable data across sites. This will enable definition of the attributes of the work of NCI PNRP navigators and allow description of the variation in navigation between different PNRP sites.

There are currently two general approaches to defining patient navigation. The first is to define the specific services navigators provide, and the second is to discuss the barriers the navigator has to address with the patient. An alternative approach to these methods is to perform observational studies and then develop a taxonomy of navigator activities. Navigators at three of the nine participating PNRP sites (Boston, Chicago, and Rochester) who support the care of patients with abnormal screening tests for breast, cervical, colorectal, or prostate cancer were observed using a preliminary observation guide. Coding of the collected data resulted in a taxonomy that defines two key dimensions: specific tasks performed and the social networks involved throughout the treatment process. The data were used to develop a conceptual observation model, which in turn led to the development of a structured observation guide.

Five types of navigator tasks were identified: navigation, facilitation, maintaining systems, documenting, and tasks not directly related to the navigator role. The first task is to navigate or work *with* patients; this includes telling, inquiring, supporting, and coaching. Telling involves explaining when and where tests will occur as well as describing the tests to the patient. Inquiring involves asking about barriers and exploring patients' concerns. Navigators support patients by listening to their fears and coach them by discussing questions they might ask their health care providers.

Another task performed by navigators is facilitation, or activities done *on behalf* of patients. This includes finding and locating patients, coordinating team communication, ensuring that patient data are documented correctly and shared with the appropriate people, and seeking collaboration.

Navigators also perform system-wide tasks that affect all patients. For example, navigators are involved in finding potential patients and reviewing logs to locate patients in need of navigation. They are also

involved in building networks and establishing routines (e.g., meeting with clinicians to explain the role of a navigator). They also review cases and follow up on open cases.

Documentation to record both actions and results is an additional task carried out by patient navigators at the three test sites. Navigators make records of their actions and the steps taken with patients. They record test results and patient data from labs, radiology, and other sources as well as other information or activities that were relevant to the navigator role. This documentation involves electronic medical records, paper records, or other formal and informal systems.

The last group of tasks identified, classified as “other,” includes tasks not directly related to the navigator role. These include research-related tasks such as obtaining patient consent for participation and collecting survey data; clinical back-up tasks (i.e., care provided outside the navigator role); and socializing and informal conversation with co-workers.

The second dimension of the study describes the social network used by the patient navigator. The first element of this network is the patient. The second element is the provider, which can be any clinical healthcare provider. The navigator also interacts with individuals and groups who provide supportive services, including the patient’s family members. Non-clinical staff who do not provide direct medical care or supportive services are also part of the navigator social network. Finally, navigators interact with medical records in order to successfully manage patient care.

The conceptual model that emerged from the collected data suggests that navigators’ tasks fall into five categories, and that there are four or more groups in their evolving social network. The variables specific to the context of each program site are the mode of contact and the type of patient. The interactions monitored were both real-time and asynchronous, and observations were taken with time sampling, since it is not possible to record everything.

In order to further improve the model, additional observations will be made at two additional PNRP sites. Each navigator will be observed four times to allow analysis of variations in tasks and networks across different navigators and program sites. The observations will be used to conduct thematic analyses of qualitative field notes in order to determine if there is a link to PNRP outcomes.

This study has produced a structured, comprehensive instrument for observing the work of patient navigators. It will allow assessment of the effects of patient navigation throughout the remaining PNRP sites and selected Avon Foundation-supported facilities.

Roles of Psychological Distress and Socio-Demographics on Development of Cancer-Related Fatigue Among Patients Undergoing Chemotherapy: A URCC CCOP Study

Pascal Jean-Pierre, University of Rochester Medical Center

Cancer-related fatigue (CRF) is a debilitating symptom that affects the psychosocial functioning and quality of life of patients undergoing chemotherapy. The reported incidence rates of CRF vary from 70 to 100 percent with an occurrence of 89 percent for individuals undergoing radiation therapy and 80 percent for those undergoing chemotherapy. The causes of CRF have been attributed to a combination of biopsychosocial factors. These factors include physiologic changes related to a malignant tumor, physical side effects of cancer treatment, and psychological correlates of cancer diagnosis and associated treatments. The purpose of this study is to examine the contributions of psychosocial distress and patient demographics to CRF.

The study was conducted by assessing fatigue in 854 cancer patients beginning chemotherapy at 23 University of Rochester Medical Center CCOP affiliates. Fatigue levels and psychological distress were assessed at cycles 2 and 4 of therapy using psychometrically valid measures. These include a fatigue symptom checklist, a profile of mood states, a brief fatigue inventory, and the Epworth sleepiness scale.

An unbiased, conditional tree analysis of collected data was conducted to examine the effects of psychosocial distress and sociodemographics on CRF.

Of those contacted, 642 cancer patients (202 males and 440 females) between the ages of 18 and 90 years provided complete data; 95 percent of the patients were white. Baseline tension or anxiety, reported cognitive difficulties, gender, and education contributed significantly to fatigue at cycle 4 among patients with low to moderate baseline fatigue. Patients' psychosocial distress and sociodemographics had no significant effect on severe fatigue.

This study indicates that psychological distress and sociodemographics influence the development of CRF. Future efforts to control CRF should consider and integrate information about the patient's psychological states and sociodemographic backgrounds.

The Role of Vitamin D and Mammographic Breast Density in Breast Cancer Risk Among Minority and Medically Underserved Women

Alecia Fair, Meharry Medical College

African Americans are known to be at high risk for developing vitamin D deficiency because increased melanization blocks the initial steps in the conversion of vitamin D from its provitamin. Fair-skinned individuals need 10 to 15 minutes of sun exposure twice a week for adequate vitamin D production; however, African Americans requires 10 to 50 times more sun exposure to produce the same amount of vitamin D. In addition, African Americans in the United States use dietary supplements less frequently than whites. Epidemiologic findings suggest that vitamin D may influence breast cancer risk through its effect on breast density, and serum levels of vitamin D have been inversely associated with breast cancer incidence. This study examines whether higher intakes of vitamin D and calcium are associated with lower breast density and whether serum vitamin D correlates with mammographic density in discriminating women with high- and low-risk breasts.

The first aim of this study is the creation of a cohort of mammography patients from the Breast Health Center at Nashville General Hospital. Blood samples will be obtained for each patient, and serum and DNA will be stored for future use. Each patient will also be examined to collect information on diet and lifestyle, anthropometric data, and skin-sunlight reflectance.

The second aim of the study is to measure the density of patients' breasts using mammography. Scans will be taken to determine both absolute and percent breast density. Breast density will be determined by digital assessment.

The final aim is to examine variation in genes critical to vitamin D production. Specifically, genes critical to vitamin D signaling (e.g., VDR and RXR), synthesis (e.g., CYP27B1), and catabolism (e.g., CYP24A1) will be analyzed. The bioavailability of 25-(OH)D3 will also be determined and correlated with breast density.

Recruitment for the study was conducted at the Breast Health Center at Nashville General Hospital, where 1,200 women annually undergo screening mammography. Approximately 60 percent of these patients are African American. The recruitment goal is enrollment of five women per week for a total of approximately 360 women after a year and a half. Currently, 27 women have enrolled since the start date of May 5, 2008. Reimbursement for participation was provided in cash, and transportation was also provided upon request.

After enrollment, each patient was interviewed to collect information on breast cancer risk factors, sun exposure, and diet. Each patient was also asked to fill out the African American food frequency questionnaire. The melanin index of each participant was measured using a Konica Minolta Spectrophotometer CM-2550d. Body fat was determined by using Lange skinfold calipers on the triceps, superiliac, and thigh, as well as measurement of the waist-to-hip ratio. Body mass index was evaluated

using a scale and height board. Breast density was quantified using the Byng algorithm once the films had been scanned and archived.

The Role of Health Literacy on Patient Navigation Intensity Prior to and Post-Prostate Cancer Diagnosis: Preliminary Results From the Patient Navigation Research Program in Chicago

June McKoy, Northwestern University

Low-income persons often face barriers when attempting to seek cancer diagnostic tests and treatment. To combat this problem, Harold Freeman implemented a novel patient navigator program in 1990 for women with abnormal mammograms. This program resulted in earlier presentations and improved survival rates. In addition, it identified specific barriers experienced by patients, including lack of insurance, poor social support, coping styles, health beliefs (e.g., fatalism), and poor health literacy skills.

Health literacy is defined as the degree to which individuals can obtain, process, and understand basic health information and services they need to make appropriate health decisions. Nearly 90 million Americans, or 36 percent of the adult population, have inadequate health literacy. Sixty-six percent of Hispanics and 58 percent of African Americans exhibit basic or below-basic health literacy levels.

The Chicago PN program is based on the Freeman model. Intervention begins at the time of an abnormal screen for prostate cancer among veterans. The aims of this program are to increase the rate of follow-up diagnostic evaluations, improve the mean time to diagnostic resolution (between abnormal screening and definitive follow-up), shorten the time to initiation of treatment following confirmatory diagnostic evaluation, and identify psychosocial and demographic factors associated with navigator noncompliance.

Three groups of individuals are involved in implementing the Chicago patient navigator model: American Cancer Society social workers; lay health navigators and trained Veterans Affairs (VA) patient navigators; and VA nursing staff. This PN team addresses issues related to the social environment and healthcare system by recording barriers to follow-up care, length of patient encounters, and case management actions. The social environment consists of support, transportation, competing roles and life stressors, and costs for care. The healthcare system's duties include patient notification and follow-up, staff training and resources, provider communication, and coordination of care. Patient interactions focus on misinformation, fear and anxiety, beliefs or fatalism, health outlook and values, means of coping and self-efficacy, and health literacy.

Patient navigators in the Chicago program follow a specific prostate patient recruitment protocol. First, the PN screens electronic medical records daily to identify eligible patients. The PN then performs a reminder call to the patient 1 day before the patient's scheduled appointment. On the day of the appointment, the PN reviews the status of patient check-in using the check-in sheet, nurses, and an inspection of the patient rooms. In order to signal eligibility for research, the PN highlights the paper check-in sheet and then waits until the doctor calls the patient's name in the waiting room. The PN actively monitors the electronic medical record from another patient room. The nurse introduces the patient to the PN, and the PN explains the program and obtains written consent and HIPAA authorization.

After a positive PSA test is recorded, an initial genitourinary appointment is scheduled within 2 to 4 weeks. A biopsy is performed 6 to 8 weeks after the initial appointment; if the pathology is positive, the patient is notified by phone in less than 2 weeks. The patient then undergoes a biopsy follow-up appointment and an education class. The time to begin treatment depends on the treatment that is given. If surgery is selected, a surgery appointment is made 4 weeks after the education class, followed by a post-surgery follow-up with the oncologist 2 weeks later. The time between the education class and the commencement of radiation therapy can be variable, but once patients undergo a consultation with a radiologist, they are scheduled for a radiation "fitting" appointment 3 weeks later. Within 2 weeks, the patient has a second consultation with the radiologist and then begins radiation therapy.

The program has currently enrolled 62 patients with a mean age of 65. Forty-eight percent of those enrolled were white and 44 percent were black or African American. Forty-four percent had an income below \$19,000, and twenty-seven percent reported that they had attended some college or had an associates degree. Forty-four percent of the men in the Chicago program had a 4th to 8th grade health literacy level as measured by the REALM-7 (Rapid estimate of Adult Literacy in Medicine) method.

Of the 62 participants on the trial, 28 eventually received a definitive prostate cancer diagnosis, and 11 patients began treatment for prostate cancer. For patients with cancer, a mean of 75 days elapsed between diagnosis and treatment initiation. Three patients opted to undergo a radical prostatectomy, three chose to utilize a combination of hormone and radiation therapy, two began radiation therapy, and two chose to watch and wait before beginning therapy.

The time navigators interfaced with patients with prostate cancer was two-fold higher than the time spent with those who did not receive a positive diagnosis. This increase in interaction included a greater median in-person encounter rate and twice as many phone encounters than with patients who had only been diagnosed with elevated PSA. Differences in navigation provision time between patients with high versus low literacy were not significant. During the study, the PNs' most common case management actions included providing emotional support and appointment reminders. The major barriers to follow-up identified were clinic-patient miscommunication, noncompliance with biopsy or preparatory instructions, and uncertainty and/or fear. The VA patient navigators' interventions to prevent these barriers included monitoring the patient's schedule to eliminate clinic-patient miscommunication, performing additional phone reminders coupled with biopsy preparatory education, and providing patient support and counseling.

Although health literacy was not a significant indicator of increased navigation intensity for this pilot cohort, improved health literacy is key to effective screening and treatment of cancer. Future studies should customize delivery of cancer care services for patients with low literacy and follow-up compliance.

Concurrent Session III-6: Clinical Trials—Progress Made in Reducing Disparities

Moderator: Wortz McCaskill-Stevens, Division of Cancer Prevention, NCI

Designing Clinical Trials for Use in CBPR Studies: Is a Different Strategy Needed?

James Hebert, University of South Carolina

The W. K. Kellogg Foundation defines community-based participatory research (CBPR) as “a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community and has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.” A community-based trial is a trial that is partially or completely delivered in the community; community members are more likely to be involved as passive recipients rather than contributors to the design of the trial. In contrast, a *community-driven* trial is one that is inspired by the community and is partially or completely designed and implemented by the community; participants may be involved in all phases and stages of the work.

Only 3-4 percent of protocol-eligible adult patients enroll in cancer treatment trials. However, at the University of South Carolina, more than 50 percent of patients have expressed willingness to participate in clinic-based, community-planned studies, many of which are lifestyle trials. The differences in acceptance rates between conventional chemotherapeutic trials and these lifestyle trials are attributed to buy-in, love, and commitment.

The NCI research continuum includes discovery, development, delivery, and dissemination. The major breakdown in this progression is often perceived to take place between development and delivery. Usually, CBPR is thought of only at the end of the continuum for purposes of outreach, but the community should be involved throughout the continuum. To do this, a safe meeting place should be created for community and academic partners to meet and learn about one another. All partners need to be able to teach and learn. The South Carolina CNP engaged its Community Advisory Group, which was enthusiastic about pursuing diet and physical activity trials. Since engaging the Community Advisory Group, a number of studies have been designed and funded. These include a colonoscopy screening trial of 900 individuals in African-American Baptist Churches in central South Carolina; a case-control study of approximately 360 individuals with adenomatous polyps and more than 360 controls; a church-based randomized intervention trial of individuals with polyps and their family members, which will look at inflammatory markers and a number of secondary outcomes; and a second round of intervention in control churches, which will use principles of peer training.

The Impact of Clinical Trials Education Program

Claudia Baquet, University of Maryland School of Medicine

The Maryland approach to health disparities features several key elements: infrastructure and community capacity; partnerships among community organizations, historically black colleges and universities, local healthcare providers, faith-based organizations, local media, and health departments; data- and evidence-guided programs; multidisciplinary research across the continuum; science-guided policy and policy research; diversity in clinical trials participation; and leveraging resources for sustainability. The University of Maryland uses a community-based infrastructure, which includes telemedicine and video linkages, to foster awareness and promote clinical trials participation.

The Maryland Clinical Trial Program conducts research on barriers faced by members of different socioeconomic, racial, or class groups. Accrual rates and trends are tracked. Healthcare professionals work with community-based professionals to promote trials in community settings; they also refer patients to trials, undergo continuing education, and participate in Grand Rounds. Training on literacy and cultural competence is provided for researchers. Numerous programs are in place for community engagement and participation. The program also carries out policy research and advocacy, and provides technical assistance for elected officials and staff.

Only 3-5 percent of cancer patients participate in clinical trials; however, a recent study showed that 32 percent of Americans would be willing to participate in a trial if asked, and an additional 38 percent might be inclined to participate but had questions/reservations. Participation among underserved populations is particularly low, and the percentage of African-American clinical trials participants is declining.

The University of Maryland performed a survey of 5,154 English-speaking, noninstitutionalized men and women aged 18 years or older with the goal of examining health behavior, clinical trials barriers, healthcare access, and screening and health status of Maryland residents. Eighty percent of blacks and 50.9 percent of whites reported that they did not know what a clinical trial is. Over 95 percent of the respondents said their physicians never discussed clinical research or trials with them. Only 11.1 percent reported previously being recruited to a clinical trial; of those, 59.4 percent participated in clinical trials. Respondents were more likely to have been recruited to a clinical trial if they were in poor health, had public health insurance coverage, or had some college or higher level education. Respondents who were informed about clinical trials by their healthcare providers were more likely to participate, as were those who were knowledgeable about clinical trials and were able to make the time commitment. Black respondents were significantly less likely to be recruited and less likely to participate in clinical trials.

Another study examined the influence of sociodemographic factors, urban/rural residence, and county-level socioeconomic factors on accrual of Maryland patients with cancer to NCI-sponsored treatment clinical trials between 1999 and 2002. Overall, more trial participants were female than male. Over the

period of time studied there were modest fluctuations in accrual for white patients but a significant decline in accrual of black patients. Accrual was highest for white female patients, followed by white male patients, black female patients, and black male patients.

The Maryland Community Clinical Trial Program was developed and conducted at Eastern Shore Oncology. The program is focused on rural community cancer center clinical trials education and availability. It utilizes a multi-pronged approach that includes community education and awareness; continuing education of physicians and other health professionals; and improved trial infrastructure. Within 5 years, there was a 20-fold increase in the number of open cancer-related protocols and a 40-fold increase in patient accrual, including many African Americans. The program has received favorable reviews from the NCI Cancer Trials Support Unit, the Eastern Cooperative Oncology Group, and other Cooperative Groups. It also received the Southwest Oncology Group award for high data quality and the HHS Best Practice Award in 2004.

Clinical Studies Outreach of the Program for the Elimination of Cancer Disparities

Graham Colditz, Washington University

The Program for the Elimination of Cancer Disparities (PECaD) is operated by the Siteman Cancer Center at Washington University School of Medicine. PECaD is a multidisciplinary, community-focused program that aims to eliminate disparities in cancer education, prevention, and treatment. It focuses on breast, lung, colon, prostate, and cervical cancer. To date, African Americans have been the primary target population of the program.

PECaD encourages community engagement in many ways. The program created a community advisory board. It carried out a study of community attitudes toward participation in research and an analysis of cancer networks and the interrelationship of providers in the community. PECaD also publishes a newsletter in the *St. Louis American*, a large African-American newspaper.

The goal of the PECaD Clinical Studies Outreach (CSO) Program is to increase minority participation in clinical trials at Siteman until participation rates mirror incidence rates for the cancers of focus. In the long term, the program would like to equalize Siteman patient demographics with those of the service region. The CSO Program is helping the community gain equal access to academic medicine and facilitating discovery of more effective treatments for all members of the community.

In 2005, when the CSO Program began, approximately 18 percent of patients at Siteman Cancer Center were minorities, while the number of minorities participating on clinical trials was only 13.7 percent. The program was implemented with the support of top management, which helped drive policy and data management changes. For example, incidence tables of Siteman cancer cases were created to help investigators determine how to target accrual of various genders, races, and ethnicities; these tables were made available through a Web site.

Follow-up with trial investigators has also been modified. Each month, the CSO team reviews new clinical studies and those up for renewal to help ensure that minority accrual targets are appropriately established and being met. Letters to investigators are written to inform them of their recruitment status, reinforce positive progress, and offer recruitment resources if needed.

Since the CSO Program has been implemented, the proportion of clinical trial participants from minority populations has increased from 13.7 percent to 15.9 percent. For the individual cancers of interest, clinical trial accrual rates for minorities are approaching or exceeding 2002-2006 cancer incidence rates at Siteman. Additional initiatives are planned to reinforce messages for providers and provide feedback to the community. Some of the lessons learned through this process are that assessment of accrual must take into account the rigidity of eligibility criteria and each study must be reviewed as an individual entity.

Eliminating Disparities in Clinical Trials (EDICT)

Armin Weinberg, Baylor College of Medicine

The EDICT (Eliminating Disparities in Clinical Trials) Project was developed to design practical and realizable policy solutions to disparities in clinical trials participation. The Chronic Disease Prevention and Control Research Center at Baylor College of Medicine is home to this collaborative endeavor of over 300 individuals nationwide, including medical researchers, healthcare professionals, patient advocates, public health officials, and pharmaceutical company representatives who worked together to develop EDICT policy recommendations. The recommendations of EDICT are designed to enhance research quality, facilitate return on investment, and distribute the fruits of biomedical research justly. The work of EDICT is guided by the following credo: (1) all individuals will have the opportunity and necessary support to participate voluntarily in clinical trials for which they are eligible; (2) participants and researchers will understand and promote the benefits of diversity in clinical trials; and (3) results from clinical research will benefit the participants' communities and society at large.

The EDICT process of policy development began with a review of medical, legal, and policy literature. This was followed by interviews with key experts, stakeholders, and partners identified through the literature review. EDICT then conducted a national roundtable to review existing data on the scope and impact of disparities in clinical trials and create an agenda for current and future policies regarding minority/underserved participation in clinical trials. Following the roundtable, policies were refined and implementation plans developed by nine EDICT Opportunity Teams—Allocation, Insurance, Professional Education, Public and Patient Education, Community, Participant Navigation, Pharmaceutical/Industry Partnerships, Publication, and Regulatory. Each EDICT team develops its policies by considering the following questions:

- v What is the problem? How does it manifest itself?
- v What would success look like?
- v Whose behavior needs to change in order to achieve the goal?
- v Who has the ability to change the behavior of the target audience?
- v What policy is recommended to achieve the behavior change in the target audience?
- v What is the feasibility of this policy?
- v What is the underlying thinking on why this policy will be effective?

EDICT also developed a Policy Context Model, which illustrates the relationship of underrepresented clinical trials participants to participating stakeholders (e.g., researchers, communities, sponsors), supporting stakeholders (e.g., insurance companies, the Intercultural Cancer Council), regulating stakeholders (e.g., IRBs, federal regulatory agencies), and influencing stakeholders (e.g., public opinion, mass media).

EDICT is pursuing a number of policies to achieve its goals. For example, regulatory changes are being proposed to improve the way clinical trials are designed and conducted. Efforts are being made to invigorate federal policies and regulations related to disparities in clinical trial participation. EDICT is seeking ways to increase collaboration between government and industry in the design and conduct of clinical trials. EDICT promotes implementation of policies that would encourage peer-reviewed journals to address representation of underserved populations in clinical trials. Other recommendations include investing in specialized training for IRB members and health professionals; reallocating research funds to avoid duplication of effort and address disparities; fostering community involvement in clinical trials; enhancing public education about clinical trials; implementing participant navigation as part of the clinical trials process; and assuring insurance coverage for costs associated with clinical trial participation.

The EDICT CLAS-ACT (Culturally and Linguistically Appropriate Services And Clinical Trials) Project helps researchers and organizations assess how well they implement standards for culturally and linguistically appropriate services in clinical trials. The EDICT BackPack Project identifies, compiles, and makes available information about policies, practices, programs, projects, and other resources that have been demonstrated to help eliminate disparities in the recruitment and retention of underrepresented groups in clinical trials.

Key Points of Discussion—Session III-6

- ✓ The type of information given back to communities that participate in CBPR and the method for providing feedback to the community depends in part on the expressed interests of the community itself. Community advisory boards should be involved in deciding how to provide feedback. The South Carolina CNP plans to hold an annual community event to present findings to the community.
- ✓ The Maryland model for addressing cancer health disparities was first developed by an individual oncologist who championed the idea within a local hospital. The program plans to expand the model for implementation in other areas. No model fits all environments.
- ✓ Researchers have been more resistant to the Maryland model than primary care providers. Researchers assume that they know everything in their area of expertise; they consider engagement with community to be “soft science.” Community-based programs must demonstrate that it can be a partner in scholarship and help promote the researcher’s career.
- ✓ CBPR training for healthcare providers focuses on design issues related to clinical trials, random assignment, reduction of bias, and phases of clinical trials. Many do not understand the role of a placebo. Training should reassure providers that they will still see their patients—referring patients doesn’t mean losing them. Providers also need to be assured that training is not costly and will not result in delays in treatment.
- ✓ The Food and Drug Administration and the Centers for Medicare and Medicaid Services are among the EDICT Project’s stakeholders.
- ✓ NCI and other federal agencies are aware of, and seeking solutions for, the barriers that IRB review and requirements for third-party observation create when working with Native American communities.

Concurrent Session IV-1: Cancer Therapeutics and Radiopharmaceutical Research

Moderator: Alexis Bakos, Diversity Training Branch, CRCHD

Genotype-Phenotype Characterization of Loss of Genomic Imprinting of IGF2-Positive Colorectal Cancer

Marcia Cruz-Correa, UPR Cancer Center

Genomic imprinting is an epigenetic form of gene silencing. Imprinting is heritable during cell division and results in monoallelic expression (i.e., expression of only maternal or paternal allele). Approximately 300 imprinted human genes have been described to date. Loss of imprinting (LOI) refers to failure of a cell to maintain this monoallelic expression. LOI associated with cancer can involve activation of tumor promoting genes (e.g., IGF2) and/or inactivation of tumor suppressor genes.

Insulin-like Growth Factor 2 (IGF2) is located on chromosome 11p15. Normally, the paternal IGF2 allele is expressed while the maternal IGF2 allele is silenced. LOI of IGF2 is found in embryonic tumors as well as in ovarian, lung, breast, and colon cancers. LOI of IGF2 is considered an independent risk factor for colorectal cancer.

The goals of the current project are to determine whether LOI of IGF2 is associated with specific clinicopathological characteristics (i.e., whether there is a LOI-positive colorectal cancer phenotype) and examine the relationship between LOI of IGF2 and response to preoperative chemoradiation therapy in rectal cancer patients. Patients who had undergone surgery for management of colorectal cancer were recruited from three centers: Johns Hopkins University, Cleveland Clinic Florida, and the University of Puerto Rico Cancer Center. Questionnaires were used to collect information on risk factors, exposure, medical history, and family medical history. Peripheral blood samples were collected for lymphocyte extraction. Differences in clinical characteristics were examined using the Chi square and Fisher Exact tests. Univariate and bivariate analyses were constructed for the association of independent covariates with LOI of IGF2. RT-PCR of Apa I-digested cDNA was used to determine LOI of IGF2.

To date, 199 patients have been evaluated. Kaplan-Meier analysis revealed that individuals with LOI of IGF2 were diagnosed with colorectal cancer at younger ages than those who did not exhibit IGF2 LOI. Interestingly, colorectal tumors in individuals with IGF2 LOI were more likely to be on the right side of the colon and were less differentiated. Patients with LOI displayed a better response to chemoradiation. These findings suggest that a distinct carcinogenic pathway exists in LOI-positive patients, which may have implications for screening, risk assessment, and disease management.

Image-Based Canine Skeletal Model for Bone Microdosimetry in the UF Dog Phantom

Laura Padilla, University of Florida

Overall, the dog is the best animal model for radiopharmaceutical research. There is a large population available and dogs spontaneously develop cancer. They are similar to humans with relation to anatomical scale, histology, and biochemistry, but have a lifespan one-seventh that of humans. One disadvantage associated with using dogs for research includes the lack of canine-specific dosimetry tools.

Unfortunately, researchers are forced to use tools based on stylized human anatomy when performing dosimetry calculations. The purpose of the current study is to construct a detailed skeletal model to complete the anatomically realistic canine phantom recently developed at the University of Florida for internal dosimetry calculations.

In order to carry out accurate skeletal dosimetry, detailed data are needed on skeletal microstructure and the masses of target regions. Different target regions will be of interest depending on the disease being studied (e.g., active bone marrow for leukemia, skeletal endosteum for bone cancer), so these regions must be distinguishable (the current phantom has a homogenous skeleton). There are four steps for developing a skeletal microdosimetry model: generating a bone mass table, macrostructure modeling, microstructure dosimetry preparation, and dosimetry calculations. A wide variety of data are needed to generate a bone mass table, including bone site volumes and densities, volume fractions, cellularity factors, and the masses of miscellaneous tissues (e.g., blood vessels, periosteum). Volume fractions were obtained for 14 bones using *ex vivo* CT imaging; cortical bone, spongiosa, and teeth (when applicable) were segmented using 3D-Doctor. MicroCT images for 12 bone samples were analyzed to obtain trabecular bone and marrow volume fractions for each sample. Efforts are underway to establish canine-specific values for cellularity, but these figures are currently being estimated.

The detailed skeletal masses obtained through this study demonstrated significant differences from the assumed mass of the homogenous skeleton; the largest difference was observed for the cranium, which was calculated to be over 39 percent more massive than predicted by the homogenous skeleton. Interestingly, it was found that active bone marrow mass represents 0.6 percent of a dog's total body weight but accounts for 1.5 percent of a human's; this difference may be due to higher extramedullary hematopoiesis in dogs.

In conclusion, the calculated homogenous bone density for the dog skeleton is approximately 15 percent larger than that of humans. The existence of canine-specific data should improve the accuracy of

microdosimetry values obtained from dogs. The skeletal dosimetry calculations for the current study should be completed within the next few months.

A Novel Glycotherapeutic for Curing Breast Cancer

Dipak Banerjee, University of Puerto Rico

At least 1 in 8 women in the United States will be diagnosed with breast cancer. Angiogenesis is a hallmark of cancer and is key for tumor growth. The balance between pro- and antiangiogenic factors is termed the “angiogenic switch.” Proangiogenic proteins include VEGF, bFGF, and IL-8, and antiangiogenic proteins include thrombospondin-1, angiostatin, interferon- α , and interferon- β . Small molecules such as cAMP can also activate angiogenesis. cAMP is known to play a role in the biosynthesis and processing of N-glycans. It promotes synthesis of lipid-linked oligosaccharides (LLOs), which are required for formation of asparagine-linked glycoproteins.

The current study evaluates the requirement for LLOs in angiogenesis and examines whether antiangiogenic glycotherapeutics could eliminate breast tumor growth. The angiogenesis model used is a nontransformed capillary endothelial cell line with preserved physiology and anatomy. Treatment of these cells with cAMP resulted in accelerated cell cycle progression, increased capillary lumen formation, and increased expression of HSP70 and HSP90. Expression of mannosylphospho dolichol synthase (DPMS), a key regulator of LLO biosynthesis, was also upregulated. Cloning and sequencing of the DPMS gene revealed a PKA motif, suggesting that DPMS may undergo PKA-dependent phosphorylation.

To further investigate the role of glycoproteins in angiogenesis, capillary endothelial cells were treated with tunicamycin, an inhibitor of protein glycosylation. Tunicamycin caused a decrease in cell surface N-glycan expression as well as a decrease in DPMS expression and activity. Bcl-2, D-type cyclins, multiple cyclin-dependent kinases, and the transcription factor E2F were also downregulated, resulting in G1 arrest and induction of apoptosis. High expression of GRP-78/Bip indicated that tunicamycin-treated cells were experiencing endoplasmic reticulum stress and inducing an unfolded protein response. Additional experiments revealed that VEGF is unable to protect cells from tunicamycin-induced apoptosis.

Tunicamycin was also tested *in vivo*; nude mice injected with breast cancer cells were treated with the agent and tumor formation was assessed. Tunicamycin reduced breast tumor growth by 50 to 65 percent when administered orally or intravenously. Immunohistochemistry of the tumors indicated that the attenuated tumor growth was due to inhibition of angiogenesis. Cellular toxicity is a concern, as it is with all therapeutics. The effects of tunicamycin are specific for the G1 stage of the cell cycle (based on *in vitro* evidence), so it should not have an effect on differentiated cells. No behavioral abnormalities were observed in tunicamycin-treated mice.

In summary, tunicamycin is a powerful inhibitor of angiogenesis that may be able to overpower tumor-derived pro-angiogenic signals. It has the potential to be a glycotherapeutic agent for breast cancer.

Key Points of Discussion

- v The principal mechanism for VEGF receptor increase is receptor phosphorylation.

2-Deoxyglucose (2DG) and Retinoic Acid (RA) as Potential Adjuvants in Combination With Molecularly Targeted Radiotherapy in Neuroblastoma

Damon Shutt, Holden Cancer Center, University of Iowa

Despite recent advances in cancer therapy, high-risk neuroblastoma remains responsible for 15 percent of childhood cancer deaths. The standard treatment sequence for this disease is high-dose chemotherapy; surgical excision of the tumor; bone marrow ablation and autologous bone marrow transplantation;

radiation therapy to the primary tumor site; and administration of retinoic acid. Even with this extensive regimen, 5-year event-free survival for high-risk neuroblastoma is only about 34 percent. The current study seeks to evaluate the therapeutic efficacy of combining a radiosensitizing chemotherapeutic, 2DG, with molecularly targeted radiation both *in vitro* and *in vivo*. The long-term goal is to develop new clinical treatment regimens for high-risk neuroblastoma patients.

Radiopeptide ligands can be tailored to target receptors on the surface of tumors; this directed approach would likely preserve normal tissue more than external beam radiation or chemotherapy. Furthermore, unlike external beam radiation, molecularly targeted radiotherapy can be used to treat disseminated tumor metastases. Modified radiopeptide ligands can also be simultaneously used as contrast agents for imaging. A radiopeptide called ⁹⁰Y-Octreotide was developed to target the somatostatin receptor, SST2.

SK-N-SH and SH-SY5Y human neuroblastoma cells were treated with 2DG with or without RA and ⁹⁰Y-Octreotide. Cancer cell killing was evaluated by clonal survival assay following treatment. Neuroblastoma cells were sensitive to a clinically relevant dose of 2DG, resulting in >50 percent clonogenic cell death within 24 hours. When ⁹⁰Y-Octreotide was administered in addition to 2DG, a synergistic effect was observed.

RA is known to increase expression of SST2, the target of ⁹⁰Y-Octreotide. It is hypothesized that priming cells or animals with RA may increase uptake of ⁹⁰Y-Octreotide by tumor cells. RA treatment of N-type neuroblastoma cells resulted in differentiation to a more S-type phenotype. Future experiments will be done in cells and animal models to test RA in combination with 2DG and ⁹⁰Y-Octreotide. If RA does facilitate increased tumor uptake of SST2-targeted radiotherapy and/or induce greater sensitivity to 2DG-induced metabolic oxidative stress, it may be a useful addition to the therapeutic regimen for neuroblastoma.

Key Points of Discussion

- ✓ The standard clonal survival assay was used for viability of neuroblastoma cells.

Concurrent Session IV-2: Patient Navigation Snapshots

Moderator: Rosemary Wong, Division of Cancer Treatment and Diagnosis, NCI

Patient and Navigator Communication: A Navigator's Applied Skill and Stories

Beverly Broadnax, The Ohio State University Comprehensive Cancer Center

The majority of patient navigation is done over the phone, and navigators rarely see patients face-to-face; thus, establishing communication lines with patients is important. The first objective is to build trust with the patient; a patient navigator should never make promises that he or she cannot keep, as funding and resources will not always be available. Navigators also need to collect information from each patient about health insurance, plans for paying medical bills, and potential barriers to getting to appointments. Navigators also need to make sure they know when and how to best reach the patient. Navigators must make sure their relationships with patients remain professional; they will not be able to solve all of the patient's problems and should focus on health-related issues. Navigators should encourage patients to be prepared at doctor's appointments. They should tell patients that it is acceptable to ask their doctor questions and call the doctor's office to obtain test results. In short, navigators should encourage patients to take control of and be proactive in their care.

It is important to establish the role of "patient navigator" at first contact with a patient and reinforce the fact that the navigator is there to help the patient overcome barriers. Once there is resolution of the patient's situation (i.e., diagnosis or cancer treatment), the navigation will end. Navigators should explain to and remind patients that they are participating in a research project, thank them for participating, and help them develop skills so they can manage their own care in the future.

Working With Male Latino Cancer Patients

Jesus Tovar, Denver Health

The role of a patient navigator is to help reduce barriers to all phases of cancer care. Navigators must have integrity and discipline, as well as the ability to set priorities. It is important that navigators feel they have chosen the right vocation. They should be confident in their ability to serve their patients and be forward-looking. By working together with health care providers and support staff, navigators can make an impact on the level of care a patient receives.

Communication is an important part of navigating, as is perseverance—a navigator must be willing to work with a patient until that person's needs are met. Navigators must have love and respect for their patients. Additionally, patients need someone who listens to them and helps them feel good about themselves. Relationships between patients and navigators are influenced by ethnicity, gender, age, and language; the relationship is best when patient and navigator share these characteristics.

Navigation training for purposes of the PNRP is difficult, because navigators need to understand screening, diagnosis, and treatment processes for breast, colorectal, and prostate cancer. The most beneficial skills for navigators include knowledge of medical terminology, since it is important to understand tests and treatments; knowledge of cancer; previous experience as an outreach worker; and knowledge of community resources. Furthermore, navigators must understand cultural issues. Among male Latino patients, common co-morbidities are diabetes, arthritis, hypertension, disability, substance abuse, mental health problems, and depression. This study will help determine whether navigation accelerates the process of diagnosis and treatment, improves the quality of treatment, and enhances the quality of patients' lives.

Trust and Satisfaction in a Northern Plains Native American Cancer Population: Walking Forward Program

Kevin Molloy, John T. Vucurevich Regional Cancer Care Institute

The goals and objectives of this program are to increase local radiation oncology research, particularly through cancer clinical trials. Patient navigators are employed to encourage participation in these clinical trials. The current study is investigating how to develop trust between Native Americans and navigators. Goals of the project are to develop a consistent model of navigation to ensure that the program is culturally responsive; incorporate culture into the program (e.g., include referrals to traditional healers); and encourage dialogue between health care providers and healers. It took 18 months for seven IRBs (including hospital and tribal IRBs) to approve the program. This process involved significant education of the tribes and engaged all levels of the tribal structure and councils. So far, the study has completed 984 surveys to assess community views, navigated 283 Native American patients, and conducted a focus group with 39 Native Americans.

The Rapid City program focuses on breast, lung, and prostate cancers, along with a few others. Most navigated patients are diagnosed at Stage III or IV. The program has found it particularly helpful to have a research nurse work with the navigators to help patients access clinical trials. The training programs for patient navigators address local health care issues; different models of training are being developed for lay and professional navigators. The program also spends time educating patients and their family members about clinical trials and works with a variety of community groups. Because the navigation program serves a rural area, distance to care facilities is a major barrier; some patients need to travel as far as 140 miles one way. This means that the navigator will have to locate services, such as dialysis and radiation therapy, that are closer to where their patients live. The program's diabetic patients often work with the diabetes nurse to make sure their diabetes is under control while they receive radiation therapy. The program attempted to translate some cancer patient literature and materials into Lakota, but because there was no way to test the translations, the initiative was unsuccessful. Next, the program plans to

promote screening and continue educating patients, conduct patient navigation surveys, and conduct clinical trials on palliation.

The NCI Community Cancer Centers Program—A Patient Navigator Aspect

Dana Coleman, Nancy N. and J. C. Lewis Cancer and Research Pavilion, St. Joseph's/Candler

After receiving a pilot study grant, the Lewis Cancer and Research Pavilion created a patient navigator position for gastrointestinal cancers. The navigator has worked with outreach groups and the 100 Black Men of Savannah group to address colorectal cancer because of the particularly high rates of the disease among black men. The patient navigation program has a mission and values system that revolves around compassion, quality of service, integrity, courtesy, accountability, and teamwork.

The Cancer and Research Pavilion uses a team approach that includes a number of physicians (e.g., medical oncologists, radiation oncologists, surgeons, internists, radiologists, pathologists), oncology patient navigators, a community outreach coordinator, a social worker, and one onsite ACS navigator. The Pavilion also has an outpatient infusion center and a palliative care clinic. There are currently three oncology navigators who cover breast, lung, and colorectal cancer. These navigators work with social workers, data managers, and clinical trial research nurses. The responsibilities of the oncology navigators are to coordinate appointments, ensure that patients understand their treatment options, educate patients about cancer prevention, facilitate trust between patients and health care providers, increase accrual to the patient navigation program, and evaluate the needs of patients as they transition from active treatment. Navigators are also involved in real-time treatment planning, as well as developing treatment summaries and survivorship plans. The position of a patient navigator is multi-faceted and continuously evolving.

The patient navigator for colon and gastrointestinal cancers works with the GI Cancer Action Team, which includes surgeons, hematologists/oncologists, radiologists, gastroenterologists, and primary care physicians. The program seeks to serve underserved populations. One of the primary modes of identifying patients is through screenings offered at free health fairs. Other patients are identified during emergency room visits or through phone calls to the care center. The navigator helps patients make the transition from diagnosis to treatment in a timely fashion and identifies available resources to address barriers that patients may encounter through their treatment.

In summary, the program strives to reduce cancer disparities by facilitating access to healthcare, reducing the number of patients who present with late stage cancers, providing prevention education materials, and offering screenings for early detection and diagnosis of cancer.

Key Points of Discussion—Session IV-2

- v Survivorship is defined as beginning at the time of diagnosis.
- v Several of the patient navigation programs described in this session work closely with regional CIS offices.
- v Patient navigators continue to interface with patients until they transition to remission or pass away. Navigators also offer pastoral care and work with local hospice providers.
- v Elderly patients often have specific needs related to health literacy. These patients are identified through an assessment process that involves asking patients to explain their understanding of what their health care provider has told them about their conditions. If these patients exhibit lack of comprehension, navigators will work to improve patient knowledge and understanding. Navigators sometimes write down questions for elderly patients to ask their health care providers or accompany them to appointments.

Concurrent Session IV-3: Tobacco-Related Research Addressing Cancer Health Disparities

Moderator: Pebbles Fagan, DCCPS, NCI

Institutionalizing a Comprehensive Tobacco-Cessation Protocol in an Indigenous Health Setting

LorrieAnn Santos, 'Imi Hale Native Hawaiian Cancer Network

'Imi Hale asked Native Hawaiian communities to prioritize their main cancer concerns and found that lifestyle issues such as smoking, diet, and exercise were often cited as important. Other concerns included timely screenings, access issues, the need for culturally relevant information, and the need for information about biological and genetic research.

Of all of the populations in Hawaii, Native Hawaiians have the highest smoking rates (24.3 percent) and the highest incidence of smoking-related diseases such cardiovascular disease, cancer, and diabetes. Of the Native Hawaiians who smoke, 40 percent reported having the desire to quit, 16 percent would like to smoke less, 26 percent have thought about quitting, 8 percent do not plan to quit at all, and 11 percent are not sure what they think about quitting. Smokers indicated concern for their children's health due to second hand smoke exposure. 'Imi Hale has institutionalized a comprehensive tobacco-cessation protocol across five different Native Hawaiian community-based health care delivery systems. The Native Hawaiian Health Care Systems have partnered with 'Imi Hale on this initiative as well as other cancer prevention and control efforts.

'Imi Hale developed an evidence-based model for tobacco cessation through a participatory process, which included interviewing smokers and former smokers to determine what kinds of information and tools could help people quit smoking. A number of materials specifically targeted to Native Hawaiian populations were developed. The first step in the protocol is to ask people about their tobacco use, then advise and assist them in quitting if they report a desire to do so. Patients who set a quit date have follow-up at 1, 4, and 12 weeks. The program attempts to take advantage of cultural pride and identification by emphasizing that smoking is not a Hawaiian tradition. Training has been provided to build capacity to implement the protocol. Also, a tobacco user guide was developed to track services provided to clients. The protocol is currently being tested by the community.

Several critical components for developing and implementing the program across multiple health care delivery systems were identified. First, the program was not only based in the community, it was also conceived in and driven by the community. In addition to its strong community ties, the program was also well organized on a larger level (i.e., links between institutions). The program is comprehensive and incorporates Native Hawaiian values and beliefs. It is also accountable to the communities it serves and fosters social norms and lifestyle changes that will improve health and well-being. The next step is to address tobacco use among Native Hawaiians as a social justice issue.

A Faith-Based Community's Perceptions of Environmental Tobacco Smoke Exposure Prevention Outreach and Partnerships

Cheryl Armstead, University of South Carolina

Passive exposure to environmental tobacco smoke (ETS) is associated with cancer and chronic diseases, especially among African Americans. Faith-based communities are viewed as potential innovators of change within higher-risk communities. In collaboration with a number of other partners, the South Carolina Cancer Disparities Community Network has initiated a qualitative pilot study called Project 2nd Hand to begin to address ETS-related disparities. The primary objective of the study is to conduct CBPR within African-American church congregations regarding ETS control and prevention. The secondary

objective is to conduct CBPR in partnership with African-American church innovators regarding the salience of ETS prevention partnerships. It was hoped that church members would be motivated to help deliver health-related messages to the larger community.

A central challenge for this project was to persuade churches to extend their outreach to communities outside their organization. Most congregations tended to want to implement programs within the church rather than conduct community outreach. Additionally, there is significant effort involved in getting church groups involved in these types of programs. First, the program must obtain endorsement from pastors and deacons, which can be difficult if these so-called “gatekeepers” are smokers. The next step is to engage with health ministries within the church, and then, finally, conduct outreach in the parochial community.

To learn more about church congregations’ attitudes and outreach capacities, a qualitative study was carried out with 40 nonsmoking African-American men and women who reported attending church regularly. Participants took part in focus groups and/or in-depth interviews and completed a survey that assessed demographics, church attendance, and smoking status. The results of the study were coded and emergent themes were derived using constant comparison methodology.

In general, respondents felt that church culture is not supportive of ETS control and education efforts, since pastors and church members who smoke tend to hide this “sin” and are often hypocritical. Also, members felt that ETS and smoking control were not a high priority; instead African Americans were focused on financial concerns, stress, and cultural traditions. The survey found that the subjects felt that apathy, lack of education, and low perceived vulnerability to ETS as the main barriers to partnerships and efforts to reduce the effects of ETS on African Americans. Respondents suggested that interventions based on traditional health education efforts would be most effective (e.g., teaching dangers of secondhand smoke in schools). African Americans who regularly attended church services as members of a congregation perceived themselves as being disconnected from African-American communities with the highest risk of cancer disparities and passive cigarette exposure.

This study has several implications. It helped dispel researcher myths about the perceived networking efficacy of churches in outreach and partnership with the larger African-American community. It found a disconnect between belief systems and health behavior within segments of the church community. It also illustrated the fact that there are intracultural differences within the African-American community. It is hoped that this study will initiate a closer examination of group dynamics as they pertain to ETS education, interventions, and policy.

Reducing Disparities in Tobacco Use Among American Indians in the Cherokee Nation: A Partnership for Cancer Prevention

June Maher, Cherokee Nation Tobacco Prevention Program

As of the year 2002, nearly 40 percent of people in the Cherokee Nation were smokers; this is significantly higher than the smoking rate among other populations. Not surprisingly, lung cancer is a serious problem for the Cherokee. In 2003, Oklahoma implemented the Oklahoma Tobacco Helpline (OTH) to help citizens of the state quit smoking. The OTH is funded by the Tobacco Settlement Endowment Trust, which also supports other tobacco counter-marketing campaigns.

The Cherokee Nation began an effort to increase use of OTH among American Indians. The goals of the current study are to: (1) learn about partnerships between a state and tribal nation; and (2) describe methods used by the Cherokee Nation to increase use of the Helpline.

The Cherokee Nation uses multiple venues to inform American Indians about the OTH. Since 2004, the Nation has paid for newspaper ads in the tribal newspaper. The State Health Department has provided free supplies to assist with marketing; representatives from the Nation assist all clinics and departments as well as local Indian Health Service hospitals with ordering and using these supplies. The Nation has also

implemented clinician training about the OTH. They have worked closely with two local organizations that are also working to reduce tobacco use throughout the community.

These efforts have resulted in progress. In 2004, only 15.2 percent of OTH callers were American Indian; by 2007, this percentage had increased to 21.7 percent. In 2005, 31.8 percent of American Indians in the Cherokee Nation were current smokers, compared with only 27.7 percent in 2006. Although it will take several years for lung cancer rates to drop, this partnership has already begun to show benefit by increasing the number of American Indians using the OTH and decreasing the disparity of smoking rates.

Increasing the Utilization of the Puerto Rico Quitline Through Outreach

Elba C. Diaz-Toro, UPR Cancer Center

The smoking prevalence rate in Puerto Rico is only 12.5 percent. However, smoking continues to be a public health burden—the five leading causes of death in Puerto Rico are associated with smoking. More than 60 percent of current smokers in Puerto Rico indicate a desire to quit smoking. The CDC-funded Puerto Rico Quitline (PRQ) provides a key cessation resource to the island.

The Outreach Pilot Project is a partnership between the M.D. Anderson Cancer Center and the University of Puerto Rico Cancer Center. The goal of the project is to use capacity building and CBPR research methods to increase utilization of the PRQ. Additionally, the Project collects data so that it can analyze which portions of the population are not being reached by its message and develop collaborations with other organizations focused on tobacco control.

These efforts have resulted in development and maintenance of a network and an outreach steering committee. Several summit meetings have been held to educate network participants and help them integrate tobacco cessation into their clinical practices. The program has developed and distributed promotional materials, started an electronic newsletter, garnered media attention, and assisted in the passage of an indoor smoking ban. The group has disseminated project outcomes in local, national, and international forums and has one paper accepted for publication. The Project will continue to integrate tobacco awareness into its programs and maintain trainings in evidence-based practices. Overall, the project has helped community leaders approach the issue of tobacco control from a public health perspective and has contributed to lowering the smoking rate in Puerto Rico from 13.1 percent in 2005 to 12.2 percent in 2007.

Key Points of Discussion—Session IV-3

- ✓ The NAACP and a cancer center in Nashville are working with churches to address tobacco-related issues.
- ✓ Some churches in South Carolina are working with community centers and other non-church programs.
- ✓ In Hawaii, recruitment of outreach workers was performed by individual health care delivery systems.

Concurrent Session IV-4: Small Business Innovation Research (SBIR) and Small Business Technology Transfer Research (STTR) Opportunities

Moderator: Emmanuel A. Taylor, Disparities Research Branch, CRCHD

General Overview of NCI SBIR/STTR Programs

Michael Weingarten, SBIR Development Center, NCI

SBIR and STTR are NCI's primary resources for enabling commercialization of innovative, high-impact technologies. Together, these programs provide \$100 million in support for activities related to NCI's mission, including research tools, medical devices, and therapeutics. They provide an incentive for academics to form their own companies based on the technologies they have developed. The company retains all intellectual property rights, and there is no requirement that the grants be repaid. Each application is subjected to a peer-review process. During Phase I, researchers are awarded an average of \$100,000 to perform feasibility studies. If results are promising, project progress to Phase II, which consists of \$750,000 awards for research and development (though the amount can exceed \$750,000 if necessary). During Phase III, customers and inventors fund commercialization of the product.

SBIR grants are specifically designed for for-profit small businesses that have less than 500 employees. The companies must be at least 51-percent U.S.-owned by individuals and independently operated or, alternatively, must be at least 51-percent owned by another business that is itself at least 51 percent owned and controlled by one or more individuals. SBIR grantee businesses are allowed to hire consultants or research institutions as partners, but the Principal Investigator's primary employment must be with the small business. SBIR has recently developed a Phase II Bridge Award because many awardees were unable to advance their technology far enough to attract private investment by the time they completed Phase II; in addition to providing funding, the Bridge Award facilitates partnerships with third-party investors who match the financial support of the award. Securing these third-party investors gives NCI confidence that the private sector is interested in the product. Third-party investors are expected to contribute rigorous commercialization guidance and additional financing beyond the initial investment. NCI intends to commit up to \$10 million to this pilot program in FY2009. Funding will initially focus on cancer therapies and cancer imaging.

STTR grants, which have smaller budgets, fund collaborations of small businesses and United States-based research institutions (e.g., colleges, universities, nonprofit research organizations, federal research entities). At least 40 percent of the STTR research project is to be conducted by the small business and at least 30 percent is to be conducted by the partnering research institution. The Principal Investigator's primary employment can be with either the small business or the research institution.

SBIR and STTR offer a joint omnibus solicitation each year that includes parent Funding Opportunity Announcements (FOAs) for both programs. Proposals submitted in response to this solicitation are due three times per year on April 5, August 5, and December 5. SBIR also issues contract solicitations, which are due in November. NIH funding opportunities, including those supported through SBIR and STTR, are posted weekly in the NIH Guide for Grants and Contracts. In recent years, NCI has been issuing more focused solicitations and investments are being targeted to technologies that are high priorities for NCI.

A strong grant application will describe significant, innovative, and focused science that has commercial potential. Applications must be clear and concise and include a summary that would be understandable to a layperson. There must be a clear plan for all of the phases, including commercialization. Applicants should be realistic about their goals and budgets and should propose feasible methods and measures of success for each specific aim. Applications should also include letters of support for commercialization. It is a good idea to contact the NIH Program Director in advance to discuss the proposal and receive

feedback. Also, applicants should consider that their proposals will be reviewed by both academic and business professionals.

Teaming/Partnership-Related Issues (Commercialization Assistance Program and Intellectual Property)

Jo Anne Goodnight, Office of the Director, NCI

The goals of the SBIR program are to stimulate technological innovation, use small businesses to meet federal research and development needs, foster participation of minorities and disadvantaged groups in technology innovation, and increase private-sector commercialization of products derived from federally funded research and development. The SBIR/STTR programs are the largest and most accessible source of seed capital for small businesses; the annual budget of the programs was \$2.3 billion in 2008. This capital is in the form of grants and contracts and does not need to be repaid.

Both SBIR and STTR have competitive three-phase programs designed to help biotechnology firms meet the challenges of developing market-ready technology (e.g., long development times, high and intense capital needs, the need for multiple rounds of financing, high burn rate of investor funds). Phase III, the commercialization phase, is supposed to be driven by non-SBIR/STTR funds; however, many investigators were having difficulty bridging the “valley of death” between Phase II development and market-ready technology. To address this, a Phase II Competing Renewal Award, or Bridge Award, was developed; this mechanism provides Phase II awardees with additional funding to continue development, conduct preclinical studies, carry out clinical evaluation, obtain approval of a federal regulatory agency, and/or make refinements to medical equipment designs. To be eligible for these grants, a business must be a Phase II awardee with a promising pharmacologic product or a device, some preclinical research in progress, and a preclinical process that requires significant resources to develop. The Competing Renewal Awards are generally \$750,000 to \$1 million per year for up to 3 years.

NIH has also established the Commercialization Assistance Program, which is currently in its fourth year. Key components of the program include workshops with advisors, mentoring from experienced “principal advisors,” an investment/partnering event, and networking opportunities. The goals of the program are to foster partnership, increase company revenue, and help businesses develop a strategic plan.

NIH has also developed Pipeline to Partnerships (P2P), a virtual space for NIH licensees and SBIR/STTR awardees to showcase technology and product development. The Web-based matrix organizes technology by disease category, application type, and phase of development (i.e., Phase I, Phase II). It also indicates whether FDA approval is needed for the technology. This resource allows potential partners to identify technologies of interest and directly link to the developing company’s Web site.

Benefits of the SBIR/STTR Programs—A Private Sector Perspective

Mary Harris, BioTechnical Communications, Inc.

Dr. Harris obtained SBIR/STTR support to develop a video program on breast cancer in African-American women. The program was first developed for cable television, but was later converted to a DVD and has since sold 8,000 copies. Her companies now utilize radio, the Internet, and interactive materials to educate African Americans about cancer.

Woman- and minority-owned firms are consistently less successful in the SBIR grant selection process, despite the fact that one of the goals of the program is to encourage participation of women and minorities in technical innovation. SBIR/STTR applications from women and minority firms have decreased from 10 percent in 1996 to 4 percent in 2006. In 2006, only 15 percent of minority applicants and 18 percent of female applicants were successful; these success rates are lower than for other applicant populations. However, these numbers should not deter companies from applying for a grant. First-time applicants have relatively high rates of success—in 2006, 41 percent of the new applicants were successful.

Applicants should know that it is not feasible for them to know or do everything when putting together a proposal. Instead, they should focus on building a strong team with expertise to perform each aspect of the project. Finances and legal concerns such as intellectual property rights are important components of business development; companies should leverage their SBIR awards to obtain other funds and retain the services of a lawyer. On the other hand, 8(a) certification is less important, and will not help secure SBIR funding. Tenacity, luck, and knowledge of the application process are integral to a successful proposal, but do not guarantee success. Other things to remember are that applications should address the interests of the agency to which they are being submitted and goals and objectives must be clearly stated.

Application Processes (Basic and Clinical Research)

Yvonne Douglas-Tabor, Division of Cancer Biology, NCI

Applicants need to ensure their proposals are consistent with the research initiatives of the Institute or Branch to which they are applying. The Division of Cancer Biology comprises the Mouse Models of Human Cancer Consortium and six Branches. The Cancer Cell Biology Branch supports research on the biological basis of cancer at the cellular and molecular level. The Cancer Etiology Branch funds research on the role of chemical, physical, and biological (e.g., viruses) agents in the etiology of cancer. The Cancer Immunology and Hematology Branch supports basic research on bone marrow transplantation, the biology of hematologic malignancies, and the earliest stages of hematopoiesis. The DNA and Chromosome Aberrations Branch funds studies of the genome, including projects focused on DNA repair; genes at the site of chromosome breaks, deletions, and translocations; epigenetic changes; and radiation- and chemical-induced changes in DNA replication. The Structural Biology and Molecular Applications Branch supports structural and molecular studies that explore the process of carcinogenesis. The Tumor Biology and Metastasis Branch provides funding for research related to cell migration, tumor invasion, and metastasis, as well as for studies on how cancer cells interact with their microenvironment. The Mouse Models of Human Cancer Consortium provides the research community with educational and informational materials related to mouse cancer models, as well as a support infrastructure. In 2007, the Division of Cancer Biology received 65 SBIR and 21 STTR applications and funded 20 and 1 of these, respectively.

Key Points of Discussion—Session IV-4

- v Unsuccessful grant applicants should closely review the summary statements they receive after their applications have been reviewed. Revised applications must address all reviewers' concerns expressed in the first summary statement, and this must be documented in the resubmission.

Concurrent Session IV-5: Grant-Writing Perspectives: Tips for Getting Your Research Funded, Research Careers (K) Through Independent Investigator (R01) Awards

Moderator: Belinda Locke, Diversity Training Branch, CRCHD

Perspectives of a Program Director: Informed Application Submission

Belinda Locke, Diversity Training Branch, CRCHD

The five major steps of informed grant application submission are selecting an Institute or Center, determining a suitable funding type, searching for an appropriate funding opportunity, contacting the Program Director (PD), and, finally, contacting the Scientific Review Officer (SRO).

Investigators should make themselves aware of the scientific mission, goals, and objectives of each NIH Institute to which they are considering submitting an application. They should also learn about funding

opportunities offered by each Institute; many funding opportunities are designed for researchers at specific levels of career development. NCI posts priorities, available resources, and funding announcements at <http://www.cancer.gov/researchandfunding>. The NCI Funded Research Portfolio, an online database of currently funded cancer research projects, can be accessed at <http://deais.nci.nih.gov/Query/>; this database can be queried by area of research, type of cancer, funding mechanism, state, and clinical trial phase.

The next step in preparing an application is to select a funding opportunity. NIH has three major funding instruments: grants, contracts, and cooperative agreements. There are four different funding avenues at NIH that include investigator-initiated research (unsolicited), program announcements (PA), requests for applications (RFA), and requests for proposals (RFP). There are also numerous NIH grant activities such as F31 (Predoctoral Fellowships), F32 (Postdoctoral Fellowships), K (Career Development), R01 (independent investigator awards), and R03 (Small Research Grant).

The Program Director is the primary contact for extramural activities and a good resource for advice and guidance on funding mechanisms and grant proposal submission requirements. PDs work in cooperation with the SRO during the review of applications and coordinate with a Grant Administrative Officer (GAO) on the allocation of funding. The PD attends Initial Review Group (IRG) meetings to help clarify programmatic issues and record pertinent application review information. The Program Director is also in charge of post-review communication, including discussing with the applicant the summary statement that cites the application's priority score and reviewers' recommendations. Program Directors are also involved in the planning of future funding opportunities.

Scientific Review Officers are federal officials who ensure that grant applications are reviewed in an impartial environment. SROs are affiliated with Center for Scientific Review (CSR) study sections and NCI IRGs and are responsible for selecting the most appropriate reviewers for each grant application. Applicants can access descriptions of CSR study sections at www.csr.nih.gov and NCI Initial Review Groups at <http://deainfo.nci.nih.gov/advisory/irg.htm>. In addition to standing study sections, NCI can also convene Special Emphasis Panels, which bring together reviewers with appropriate expertise for review of specific applications on an *ad hoc* basis.

There are several typical application deficits that compromise a proposal's chance of being funded. Many unsuccessful applications suffer from lack of details on the project and are not well written. Other proposals are not funded because they are overly ambitious, too descriptive instead of hypothesis driven, or contain an incomplete literature review. Candidates should be careful to distinguish between what they have accomplished themselves and their laboratory's accomplishments.

After a grant is selected for funding, grantees and their home institution may need to interact with an NIH or NCI Grants Administrator Officer who coordinates requests for "Just-in-time" information. This is information that is requested after review of the application, but before funding is awarded. Information requested may concern human subjects, animal subjects, budget issues, and other support. The GAO works in coordination with the PD and other NCI staff.

Additional Web sites that may be helpful in the grant application process include the following:

- ✓ Computer Retrieval of Information on Scientific Projects (<http://report.nih.gov/crisp.aspx>)
- ✓ Tips for New NIH Grant Applicants (<http://www.nigms.nih.gov/Research/Application/Tips.htm>)
- ✓ Planning Your Application (http://grants.nih.gov/grants/planning_application.htm)
- ✓ How to Write a Grant in Cancer CAM (Complementary and Alternative Medicine) (<http://www.cancer.gov/cam/attachments/howtowrite.pdf>)
- ✓ NCI Everything You Wanted to Know About the NCI Grants Process But Were Afraid to Ask (<http://www3.cancer.gov/admin/gab/index.htm>)

- v Insider's Guide to Peer Review for Applicants (<http://cms.csr.nih.gov/ResourcesforApplicants/Advice.htm>)
- v NIH Telephone and Service Directory (<http://teledirectory.nih.gov>)

Perspectives of a Reviewer: Communicating Your Science

John Ojeifo, Georgetown University Medical Center

When performing reviews of grant applications for both independent investigator awards (R01) and career development awards (K), reviewers look for specific criteria as well as common application mistakes. Knowing these criteria and application mistakes will assist new investigators in preparation of a solid grant application.

An R01 research project is evaluated using five criteria. The first criterion used by the review committee is the significance of the proposed investigation, including the relevance of the problem the study will address (e.g., the medical and/or health significance of the research plans or the relevance to a particular medical problem). Reviewers also evaluate how scientific knowledge or clinical practice will be advanced if the specific aims of the application are achieved. The significance of the proposal also includes the effect of the study on concepts, methods, technologies, treatments, services, or preventive interventions that drive the field of study.

Reviewers also evaluate the experimental approach proposed in the application to determine if the conceptual or clinical framework, design, methods, and analyses are well reasoned, well integrated, adequately developed, and appropriate for the study. The applicant's knowledge of potential problems and alternative tactics is also evaluated. Additionally, reviewers also carefully consider whether the application adequately addresses the safety and welfare of any human and animal subjects that will be used in the research.

Reviewers also assess the innovativeness of the research plan. They consider the originality and novelty of the project and determine whether it challenges existing paradigms or clinical practice. Candidates are also evaluated on whether the project addresses innovative hypotheses or critical barriers to progress in the field, and on how they develop and employ novel concepts, approaches, or methodologies for a particular field or area.

The qualifications and track record of the applicant is also a consideration in the review process. The suitability of the project is gauged against the experience level of the investigator and collaborators. Reviewers also determine the complementary and integrated expertise brought to the project by the investigative team.

The final evaluation criteria used for review of grant applications is the scientific environment in which the project will occur. Reviewers assess whether the environment will contribute to the success of the study or if there are unique features of the scientific environment, such as subject populations or collaborative arrangements. Another important parameter is the level of institutional support for the proposed project.

Overall, reviewers look for highly significant projects with original and novel concepts and approaches. It is beneficial if the proposal incorporates current scientific research concepts and the investigator has a strong scientific background. Well articulated scientific ideas and a well-presented research plan will stand out and increase the proposal's chances for success. Clearly stated research problems, goals, and specific aims assist reviewers in assessing the merits of the project. Environments with unique features and strong institutional support should be emphasized.

Career development research projects have different evaluation criteria than R01 applications. These applications are evaluated on the research plan; candidate; reference letters and statements from mentor (or former mentor); and the environment. Originality and scientific merit of the research plan are very

important. Reviewers assess the extent to which the study plan tests new concepts and ideas and the medical or health significance of the research.

Candidates are judged by their education, training, and the quality of their mentored period of cancer research training. Scientific productivity is an important criterion for career development awards. Reviewers attempt to assess the potential ability of the candidate to successfully manage an independent research project. Any special skills that the candidate possesses should be emphasized to help the review committee determine if the candidate is qualified to accomplish the research goals of the investigation.

Letters of recommendation from former mentors and collaborators are judged by the strength of the recommendations and the qualifications of mentors in their respective research fields.

Finally, the committee determines the quality of the environment for scientific and professional development. Factors such as the proposed research facility and the track record of the institution in cancer research are considered. Inclusion of documentation of a well-established research program in basic, clinical, and cancer research will enhance an application. It is also important to adequately and clearly detail the institution's assurance that the investigator will spend a minimum of 75 percent of full-time professional effort on the proposed career development plan.

There are also some unwritten evaluation criteria that most reviewers employ. Good grammar and spelling are key. A well-organized format and concise, easy-to-read writing style are very important. Applicants should include simple, uncluttered, and interesting diagrams and graphics to emphasize important points. Reviewers will be more likely to understand and remember key points if they are concisely presented and repeated throughout the proposal.

Some common mistakes can affect the outcome of a grant application. Research that is neither exciting nor new, or lacks a compelling rationale, will adversely affect a successful outcome. If a project leads to only incremental advances or has low impact on the field of study, it is considered a poor application. Another common mistake is failure to describe the biomedical relevance of the project.

Poor applications often have problems with the specific aims of the project. For example, unfocused specific aims and lack of a provable hypothesis will negatively affect the review of the proposal. Many proposals are too ambitious, outlining work that would be impossible to complete in the proposed time frame with the resources available. Limited specific aims and uncertain future directions are also mistakes that should be avoided when preparing a grant application.

When describing experimental procedures in a grant application, it is important to establish the feasibility of each specific aim with preliminary data. It is a mistake to propose experiments that do not directly test the hypothesis or are not directed toward the mechanism being evaluated. Applicants should clearly describe the approaches they plan to use but avoid providing too much unnecessary experimental detail. Preliminary data should be shown to establish feasibility of the proposed experimental approach and demonstrate expertise. One should not use correlative or descriptive data. It is important to discuss the method of data analysis (including statistical analysis) and interpretation that will be employed during the study and detail potential pitfalls and alternative strategies that can be substituted in case of problems.

Several problems can occur regarding the proposed principal investigator. For instance, it is sometimes unclear whether the proposed project will be led by the applicant or a collaborator. There are also problems when an applicant does not demonstrate the expertise needed for a particular method. Low scientific productivity will also reflect badly on an investigator. Failure to recruit collaborators or omission of letters from collaborators describing the planned partnership can detract from an application.

If there is little demonstration of institutional support, it may be difficult to obtain funding for a grant. Lack of investigator access to facilities or equipment necessary to carry out the proposed research will also detract from an application.

There are guidelines investigators can follow to better communicate their science to reviewers. First, it is important to remember that reviewers are volunteers with many applications to evaluate. Applicants should always read and follow prescribed formats and instructions, keeping the text of the applications short, to the point, and interesting. It is also important that the flow of the application is logical and the scientific problem clearly and prominently stated. Credit should be given to others in the field, when appropriate. Investigators should emphasize their credentials to perform the research and the potential value of the proposed study to its field. Proposed research should be placed in context and compared and contrasted with other research. A viable research plan should be developed with research objectives carefully formulated and clearly stated. Proposals should be thoroughly proofread by several individuals to avoid grammatical and spelling errors and possible omissions. Grammar and spelling can lead to ambiguities that make the proposal difficult to read and understand. Applicants should consider the use of organizers to simplify the cognitive load and tables for complex material. All abbreviations and acronyms should be defined at first use. Text should be written in everyday language; jargon and unnecessary technical terms should be avoided and an active rather than the passive voice should be used. Specific adverbs and pronouns that clearly refer to a specific noun should be employed. Introduced terms should be used consistently and important points should be repeated for emphasis.

Perspectives of a Successful Applicant: Challenges and Triumph!

Carlos de los Santos, State University of New York at Stony Brook

When applying for research funding, a good research idea is necessary, but it is not enough. Acquiring funding from the NIH has become more difficult in recent years, and this is especially true for new investigators. In fiscal year 2007, approximately 22 percent of Research Project Grants and 24 percent of R01 equivalent applications were awarded. Between fiscal years 1998 and 2007, success rates of new R01-equivalent applications were higher for previously funded investigators than for first-time investigators. There is a category of career development awards (K funding mechanisms) that is directed towards scientists at the beginning of their careers. In fiscal year 2007, success rates for K awards ranged from 30 percent to 48 percent.

There are strategies to help improve an applicant's chances for success. The first, and most important step is to have a good idea. It is crucial to identify a mentor to help evaluate the idea and provide advice on how to proceed. For all applications, except R21 proposals, it is necessary to generate preliminary data. Even in cases where preliminary data are not required, showing study feasibility will strengthen an application. The next step is to seek collaborators who can assist in reaching investigation goals and then obtain letters from them confirming their commitment to the project. Lastly, the NIH and CURE staff should be contacted to assist in finding the appropriate grant mechanisms.

Applicants should leave themselves plenty of time to write a proposal. It is important to demonstrate knowledge of the current literature and state of the science in the field. If the proposed study will address gaps in current basic or clinical knowledge, these should be highlighted. Specific aims should be focused, and possible outcomes, potential problems, and available alternatives should be discussed. The application should be made reviewer-friendly by use of concise writing, readable fonts (not the smallest margins and fonts allowed), paragraph breaks, and figures to illustrate complicated points. Careful proofreading of the application is crucial, as is conveying enthusiasm for the project.

Before the application is submitted, it should be read and critiqued by senior investigators and directed to a "friendly" study section that will understand the application.

If the proposal is not competitive when first submitted, investigators must be persistent. A call to the Program Director, as well as asking senior investigators to read the summary statement can help identify weaknesses in the application. Guidance from these sources can help investigators develop a revised application that addresses reviewer critiques. With an award success rate of 30 percent, most investigators

will need to submit three applications before getting funded. For more information on grant writing tips see http://grants.nih.gov/grants/grant_tips.htm.

The NIH/NCI Review Process—An Overview

Sonya Roberson, Research Training and Review Branch, NCI

A study section is typically composed of 20 or more members. These members are senior investigators in a range of related fields and are selected primarily from academia. In general, 40 to 100 applications are reviewed at a study section meeting, which lasts from 1 to 2 days. The Scientific Review Officer opens the meeting with an orientation on the policies and procedures involved in the review process.

The review process is used to assess the technical and scientific merit of grant applications and to assign merit scores to each. Each individual application is reviewed on its own merit. Study section members do not make funding decisions; however, results from the review deliberations provide essential information to program staff as they make their funding decisions. Actual funding comes much later in the review process. Issues such as funding and pay lines should not be discussed during the proceedings.

Two important principles of review are conflict of interest and confidentiality. A conflict of interest occurs when a reviewer has an interest in the grant application that may bias evaluation of the project. This interest could be employment, financial benefit, or a professional or personal relationship. Conflict can be real or apparent. If a reviewer is in conflict with an application, the individual will be recused during the review of that application.

All matters, including the application and deliberations, are kept confidential. Everything in the application, except those items that are in the public domain, is confidential. Reviewers should not engage in conversation or discussion with any applicant at any time regarding an application review. Applicants with questions or issues should be referred to the SRO of the study section, and any efforts by an applicant to contact a reviewer should be reported. The review process is not completed until the National Cancer Advisory Board meeting for a particular round has concluded.

Until recently, NIH used the Central Contractor Registration (CCR) to reimburse peer reviewers for their time and expenses; however, this practice is being discontinued in accordance with a General Services Administration directive. An interim solution has been adopted through September 30, 2008. If reviewers registrations are active, they will continue to receive payment through direct deposit. If reviewers are not registered with CCR or if their registrations have expired, they will receive checks from World Travel Service. The checks will be mailed to the residential addresses on file in the NIH Commons. Reviewers should not renew their CCR registrations upon expiration, and they should ignore e-mails that prompt renewal of registration.

Each member of a study section has a specific role to play. The SRO is the designated federal official for the review meeting. The job of the SRO is to explain NIH policies and procedures and review guidelines and criteria, as needed. The SRO also works with the study section Chairs to direct the overall review. At the end of the meeting, the SRO prepares summary statements based on the discussion and reviewers' written critiques.

The chairpersons of the meeting assure that the review is free from bias and that equitable time is allowed for discussion of each application. It is also the chairperson's duty to keep reviewers focused on the application's merit and ensure that all review criteria are addressed. Finally, the chairpersons ensure the review process proceeds in an expeditious manner by maintaining a timeline and requesting a summary if there is extended discussion on a particular topic.

Reviewers are asked to evaluate applications based on their own experience and standards of quality, but should also listen to other reviewers' opinions with an open mind. At the end of the review, assigned reviewers have an opportunity to revise their preliminary critiques based on group discussion.

Program staff are present during the review to monitor scientific progress made on grants and contracts. They also make funding decisions and manage the program if funds are awarded. The staff are also present in order to listen to discussions and assist in explaining the outcome to applicants.

Applications are assessed according to five review criteria: significance, approach, innovation, investigator, and environment. Reviewers are asked to consider the following questions related to each criterion:

- v **Significance:** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?
- v **Approach:** Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well-integrated, well-reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? Are plans to coordinate among multiple principal investigators adequate?
- v **Innovation:** Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice or address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?
- v **Investigator:** Are the investigator(s) appropriately trained and well-suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator(s) and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?
- v **Environment:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

A project does not have to be strong in all categories in order to be judged to have a major scientific impact. For example, a clinical trial may not be innovative, but it may have a high impact on the field. The final evaluation should reflect a balance of the application's strengths and weaknesses. Reviewers' critiques should be based only on the information that is in the application. No special exceptions can be made for an applicant known to be outstanding in his/her field when reviewers deem the submitted application to be inadequate. Other factors that should be discussed by the study section, including issues related to human subjects and animal welfare, may or may not impact the merit of an application. Merit scores should not reflect issues related to data sharing or budget, but administrative notes can be included in the review to reflect reviewer concerns.

Internet Assisted Review allows reviewers to perform several tasks online. Reviewers can submit critiques and preliminary scores prior to a meeting and review critiques of other participating reviewers. After the meeting takes place, it is possible to modify posted critiques based on the meeting discussion. The ability to post critiques in advance facilitates discussion at the actual review meeting.

Amended applications are also reviewed during study section meetings. Reviewers are asked to evaluate revised and resubmitted applications in light of recent scientific advancement and to take into consideration the applicants' responses and any new or old issues that were not addressed in the prior review. Amended applications are scored from a new starting point and may score better, the same, or worse than the original application.

Preliminary scoring of an application is based on the enthusiasm of three assigned reviewers for the project. Reviewers are not bound to keep these scores. Preliminary scoring is followed by discussion of

the application by the entire study section, and the assigned reviewers are then asked to finalize their scores. The full group then votes, and assigned reviewers are asked to modify their initial critiques to reflect any changes in scoring.

Scores can range from 1.0 (highest merit) to 5.0 (lowest merit). The numerical rating can be anywhere within this range in increments of 0.1. Scores will provide the major basis of funding decisions. It is imperative that scores are suitably spread out to ensure meaningful distinction between applications that differ in merit. The range of scores is particularly important because of the tight funding environment. If all scores are compressed, it is difficult for program staff to discriminate among rated applications.

A streamlining process is in place to allow study sections to spend their time discussing only those applications that have the highest merit. Applications deemed by the assigned reviewers to be noncompetitive are not discussed during the meeting and are not assigned a priority score, although if any reviewer feels that a particular application should be discussed, it will be placed on the agenda for discussion. Although applications deemed noncompetitive are not discussed during the meeting, this does not mean that they lack scientific merit.

In an effort to encourage team science, applications can now be associated with more than one principal investigator. Principal investigators are expected to share responsibility for directing the project or activity. A leadership plan is required, which should describe the governance and structure of the organization. This plan should define communication plans and decision-making methods that will be employed. Procedures for resolving conflicts should also be outlined in the application. This plan is evaluated under the approach criteria and does impact the merit of the application.

NIH is converting from paper applications to an electronic submission process. The new process involves two systems—Grants.gov, an online portal for identifying opportunities and applying for grant funding from all federal agencies, and the NIH electronic Research Administration System (eRA Commons), the NIH system for receiving and transmitting applications and award information. In order to use this system, an applicant's institution must be registered with Grants.gov, and both the institution and individual investigator must be registered in eRA Commons. Most single-component research project grants (R series award mechanisms) have already transitioned to an electronic format. Career development (K series) applications are scheduled to transition to electronic submission in early 2009. More information on the transition to electronic grant submissions can be found at <http://era.nih.gov/ElectronicReceipt>.

In order to be submitted to Grants.gov, applications must be in response to an open Funding Opportunity Announcement. The NIH Guide for Grants and Contracts provides a link to the correct FOA for each NIH Program Announcement and Request for Applications. Application packages containing the appropriate forms and instructions for a specific FOA can be downloaded from Grants.gov. Investigators should download a new application package each time they submit a grant to ensure that they use the most current version of the required forms. Electronic grant applications must be submitted by authorized institutional officials. Submissions are electronically validated by both Grants.gov and eRA Commons and applications with errors are rejected.

Concurrent Session IV-6: Grant-Writing Perspectives: Tips for Getting Your Research Funded Through Small Research Grants (R03) Awards

Moderator: Audie Atienza, DCCPS, NCI

Perspectives of a Scientific Review Officer

Ellen Schwartz, Center for Scientific Review, NIH

Researchers will likely be able to prepare more successful grant applications if they understand the grant review system and the sequence of events that occurs once a grant has been submitted. Once a researcher writes and submits an application to NCI, it undergoes a peer-review process. NCI reviews some of these applications, but most are reviewed by the NIH Center for Scientific Review, which functions as a service institution for more than a dozen NIH Institutes and Centers (ICs).

When a grant is submitted, the application is assigned to an NIH Institute and a Division within that Institute. Division staff assign each submission to the appropriate study section; study sections are formally called Scientific Review Groups (SRGs). The application then goes to a Scientific Review Officer. The SRO reviews the range of applications and assigns three reviewers with appropriate expertise to each application. Reviewers read the grant application, write a critique, and assign a score. Only submissions deemed by the primary reviewers to be among the top 50 percent of applications are discussed at the Scientific Review Group (SRG). All applications that are discussed at this meeting are assigned a new priority score. A summary statement is prepared and forwarded to the applicant and IC along with the application's priority score. No funding decisions are made at the study section level. Members of the SRG attempt to review the grant applications without consideration of where the payline will be in different ICs.

The grant then undergoes a second level of review by the appropriate IC Advisory Council; for NCI, this is the National Cancer Advisory Board. This group assesses the quality of the SRG review and evaluates the grant applications. The Advisory Council then makes funding recommendations to IC staff. They also evaluate funding program priorities and relevance as well as advise on policy.

The core values of peer review at NIH are to provide a competent, thorough, and fair review of grant applications. Most study sections cover multiple scientific areas within the context of a common theme, and SROs therefore recruit reviewers from a variety of related disciplines. Without the dedicated efforts of these volunteer experts who serve as reviewers, NIH could not fulfill its mission to improve the health of our citizens through biomedical research.

Applicants preparing to submit a grant application should be cognizant of certain important guidelines. First, it is imperative to carefully read and follow directions as posted on the NIH Web site. Next, talking with Program Officers is important as they serve as guides to investigators and have observed many study section meetings. Their insight into the grant review process can be very helpful, and they are willing to share their knowledge with investigators. Additionally, applicants should select relevant information carefully in order to make best use of the permitted page space. Key elements of the grant that tell the story (e.g., what, why, how, where, and who) should be addressed. Finally, advice from mentors and other experts in the field should be solicited. Applicants should view the grant submission process as an opportunity to expand professional networks and develop relationships with additional mentors.

There are five key criteria on which reviewers are asked to score all research applications. These criteria have been developed in order to provide a level playing field for all grant applicants. The first criterion is significance, and an increasing emphasis is being placed on this category. It is important that the grant be clear about how the proposed research is expected to advance scientific knowledge or clinical practice. Next, reviewers evaluate the approach outlined in the grant. The conceptual framework should be clear

and linked to plans for data collection and analysis. It is important to point out specific ways in which the research is innovative. Finally, the members of the study section assess the investigators and the environment of the research proposal. After evaluation of each of these criteria, reviewers determine an overall score that reflects the scientific and technical merit of the application.

There are some other key issues to keep in mind when preparing a grant proposal. First, the abstract is an important first impression for reviewers and should focus on key aims and methods in addition to the justification for the proposed research. Also, investigators are given two opportunities to revise and resubmit a proposal. If a grant is to be revised and resubmitted, it is important to talk to the program officer and to respond to reviewer comments, even if the suggested changes are not included. The introduction section of the grant can be used to note the changes made during the revision process.

Building Your Research Portfolio

Heather Brandt, University of South Carolina

Research begins with an idea. In addition to being meaningful and leading to advances in the field, the idea should be one for which the researcher has passion. Participating in other activities, such as serving as a temporary reviewer of grant proposals, may allow a researcher to gain experience related to the process of obtaining research funding. As a grant reviewer, the researcher has the opportunity to hear from senior level researchers and better understand what NIH is looking for in research proposals. Many opportunities are available for reviewing outside NIH (e.g., American Cancer Society, Lance Armstrong Foundation, Susan G. Komen for the Cure). Reviewing abstracts for journal articles is also helpful. Participating in these activities can help researchers develop new ideas and improve critical thinking.

Developing ideas into a single project and eventually a research program can seem overwhelming. Building a research program includes expanding and conceptualizing ideas into a research plan. Both classroom and mentored experiences can assist an independent investigator in building a foundation for a research program. Also, the use of small funding mechanisms on a local level allows new researchers to gain experience and begin to build their own programs.

Good mentorship is essential. Researchers should take advantage of opportunities to learn from others through research and professional service (e.g., reviewing abstracts, manuscripts, or grants) as well as forming collaborations with senior scientists. If a relationship with a particular mentor is not positive, researchers should select another and consider having more than one to provide differing perspectives. Peer mentors can also be as important as senior mentors. The best mentor is not necessarily the most senior person. It is more important to have a mentor who is available and can provide time and assistance.

Investigators should persevere and be open to constructive criticism. They should also be inquisitive and continue to ask questions and challenge existing paradigms. Evidence-based approaches are only as solid as the foundation on which the evidence was built. Investigators should avoid being encumbered by fear of the NIH, failure, blazing new trails, asking questions, criticism, saying no, null results, or protecting one's time from research.

Formulation of the Research Question

Wenchi Liang, Georgetown University

The Asian Tobacco Education and Cancer Awareness Research Initiative Community Networks Program pilot study investigates the effectiveness of physician-based intervention to increase colorectal cancer screening among Chinese patients.

The pilot study has three specific aims. The first is to develop a physician-based intervention aimed at improving physician communication and recommendations regarding CRC screening. The second is to evaluate the feasibility and acceptability of the intervention. Lastly, the study will be used to assess the

impact of the intervention on CRC screening intentions among Chinese American patients nonadherent to CRC screening guidelines.

To accomplish these goals, four primary care physicians (two at each site) were assigned to an interview or control role. One hundred Chinese patients were enrolled. The patients were 50 years and older and did not currently participate in CRC screening. For the physician's intervention, CRC materials were printed and two in-office physician-training sessions were held. Data on the interactions were collected through the doctor's process evaluation and a patient post-visit survey. This information was used to measure self-reported patient CRC screening intention, and medical chart review was used to assess patient behavior.

In-office training for physicians included role-playing of the doctor-patient interaction in specific scenarios. The interviews took approximately 30 minutes, and a CRC communication rating was immediately given to the doctor at the end of the session.

Although the community-based intervention was culturally appropriate, its effectiveness was limited. To follow up on these results, the research team is applying for R01 grant support to carry out a longitudinal study to evaluate the effectiveness of the physician-based intervention in improving Chinese-American patient's actual CRC rates. The CNP pilot study results will be used to revise the physician-based intervention and recruitment strategies. For example, additional physician training sessions will be included. Also, flip charts and laminated summary tables will be provided for the interview, and chart review and patient selection procedures will be enhanced.

Some noteworthy points were identified while planning the current CNP study and the subsequent R01 grant. First, it is important to assure interest in the question being asked, as the research will be ongoing for several years. Also, researchers must determine if the population is interested in solving the problem that has been identified. Since funding is limited to 3 years, it is necessary to have a topic that is not too broad or too specific. In addition, consideration should be given as to whether the results of the study will add new knowledge to the field; applicants must establish what has already been done and determine where gaps exist. Researchers should also consider whether the research question could be answered in a timely manner before information becomes irrelevant. Additionally, consideration should be given as to whether good collaborators and mentors can be located and whether the answers to the research question will lead to meaningful next steps. Finally, consider whether funding sources will be interested in the research question and consider how best to sell the project to them. Obtaining funding through the R03 or another small grant mechanism may be a good way to accumulate data that can later be used as the basis for an R01 application.

Concrete Steps to Prepare Your Application

Jeanne Mandelblatt, Georgetown University

The first section of a grant describes the specific aims of the research. This section is 1 to 1.5 pages in length and should describe the entire project in an abbreviated form. The reviewer should be able to read the Specific Aims section and understand everything about the project. A well-written aims section should orient the reader for the entire application.

The first paragraph of the Specific Aim sections should define the importance of the problem. The proposal should then become more specific in describing each particular aspect of the problem that will be investigated. The current state of the field should be defined and the existence of gaps in knowledge highlighted.

The second paragraph should describe the research question as well as prior work that supports the focus and feasibility of the project. Theoretical models that will be used to guide the work should be outlined. The research plan should be carefully described and important members of the research team identified.

In paragraph three, the specific aims of the project should be presented. Each aim should be stated as a declarative sentence followed by a theory-driven hypothesis. The proposal should be limited to one

primary and one or two secondary aims. Aims should logically flow from information already presented. It is important to focus on a hypothesis that will guide future work and to make the next steps obvious.

The fourth paragraph of the Specific Aims section is the summary. The summary should describe the innovativeness and importance of the proposed research and illustrate how the project will address NIH's top priorities. The summary should also explain why there is a high probability of success for the project and how the experience on the project will contribute to the investigator's career development.

The second section of the grant proposal, Background, should be three pages in length. It may be easier to write this section after the rest of the grant has been prepared. The first paragraph of the Background section introduces the scope of the problem and should flow from general to specific. It details gaps in the field and the rationale for the study. This paragraph is used to explain what the study will do and why it is important. It allows the researcher to present the organization of the rest of the grant.

Paragraph two of the Background should provide the conceptual framework of the proposal. It is important to select a well-known model with clear relationships and describe why the model is well-suited to your question and how has it been applied in the past. Researchers should explain how the model will be adapted to the research project; what it suggests; how it supports the research; and how it will support future work. A figure of the model with the specific aims and leverage points for future interventions highlighted is very useful.

The next three paragraphs of the background section should contain a literature review organized by model terms. Reviewers should highlight literature on key model predictors and stress how the model informs the experimental design. This section should also include literature on key mediators, controlling variables, and the primary outcome. At the end of each paragraph, a summary of the important points that support the research idea should be included.

The last paragraph of the Background should present a detailed summary of the significance and innovation of the proposed work. The main selling points of the proposal (e.g. importance, novelty, investigator, team, and environment) should be clearly stated using an active voice for more effective presentation.

The third section of the proposal describes the preliminary studies that have been performed; this section should be one to two pages in length. The Preliminary Studies section demonstrates that the proposed research is feasible. The first step is to introduce the section and then delineate the research, followed by a description of what the lab or mentor has already accomplished and how the work suggests the feasibility of continued study. It is important to stress collaborations with the mentor and other members of the research community and provide examples of how the environment will promote the study. The summary of the Preliminary Studies section should highlight the importance of prior work accomplished, the team of researchers, and the environment to achieve a high probability of success for the proposed investigation.

The Methods section, which comprises the bulk of the proposal, should be nine to ten pages in length. Figures are important in this section to clarify the process. The introduction should provide an overview of the project, a figure illustrating the process, and an explanation of how the work relates to the career goals of the author. The two major parts of the Methods section are design considerations and the timeline and organization for the project.

Justification of the experimental design is one of the most important parts of the Methods section. This part of the proposal informs reviewers of potential problems and describes the rationale for using proposed methods. Early in the justification, differing experimental approaches should be outlined and accompanied by support for the approach that is deemed superior. Examples of design considerations include alternative approaches; selection biases and representation; choice of endpoints and definition of the gold standard; choice of data collection time points; possible changes in practice; how choices relate to usual practice; and the balance between practical and theoretical considerations. It is also imperative to

define the population that will be studied. The application should indicate how many subjects will be involved in the research as well as whether the sample will be representative. Examples from prior work should be used to explain the expected consent process and demonstrate that achieving the proposed sample size is feasible within the specified time period. Clarification should be made for how subjects in the study will be recruited, and an outline of previous experience and success in the recruitment process should be provided (letters of support from mentors or collaborators may help establish experience and prior success). A description of recruitment incentives and retention strategies to be employed should be included, as well as the literacy level for materials to be distributed.

Once the choice of research methods has been explained and validated, a description of data that will be collected should be provided, including details on what will be collected, from whom, when, where, and how long it will take to complete data collection. This approach must be backed up with pilot data that supports the feasibility of the method. Attention should be paid to how the data will be managed, including Health Insurance Portability and Accountability Act (HIPAA) compliance; security of patient identity; de-identification; and storage of identifiers. When discussing analysis of collected data, researchers should also address statistical power and other issues related to the choice of the analytical approach. A detailed analysis method for each specific aim of the study should be included. Finally, a good statistician should carefully proofread the analysis plan.

The last section of the proposal is the Summary. This section should contain a description of the project's strengths and limitations as well as its importance to the field of research. The contribution of the research to the investigator's career and training should also be stated. Examples of next steps in the project should be outlined and linked to specific aims and results obtained. An attempt should be made to emphasize how the project will move the field forward and contribute to the health of the population.

General pointers for improving the quality of an application include:

- ✓ Carefully read the provided instructions and ensure that the proposal addresses review criteria.
- ✓ Use successful grant applications as models.
- ✓ Write the specific aims of the proposal first to help keep the application focused.
- ✓ Accentuate important points by including them in the first and last sentences of a paragraph.
- ✓ Employ an active rather than passive voice, incorporating short sentences that are easy to read.
- ✓ Seek qualified outside reviewers and editors to proofread and critique the application
- ✓ Make sure that the application is as neat and concise as possible.

Overview of the Small Grants Program for Behavioral Research in Cancer Control

Veronica Chollette, Applied Cancer Screening Research Branch, NCI

The small grants program for behavioral research in cancer control was first issued in 1999. The program has been reissued five times, which emphasizes NCI's commitment to fund this type of research. The program has several goals: (1) enable investigators to collect pilot or feasibility data; (2) support a variety of small-scale projects with simplified application procedures; (3) enable new investigators, or those from institutions without well-developed research traditions or resources, to begin independent research activities; and (4) increase the total number of Research Project Grants and decrease the average per-grant cost. The pilot and feasibility grants are only ten pages long and are designed to increase the likelihood that an investigator will be funded at a higher level in the future.

There are many small research, or R03, grant programs across NCI and NIH. Each is associated with a specific program name and number. The NCI Behavioral Research Program small grant programs is unique because it provides support for up to 3 years (traditional R03 are only 2 years in duration). If an R03 study was planned for 2 years, but more time is needed, it is possible to request a no-cost extension

for an additional year. Applications are accepted in the areas that reflect the interests of NCI and awarded using just-in-time procedures. Applicants are permitted to revise and resubmit their applications twice. Eligibility requirements are different and designed to attract new and junior investigators. Investigators who have already received an R03, R21, P21, or R01 grant are ineligible for the program.

In order to determine if the program is achieving its goals, data from grantees and mentors were collected for evaluation of the impact on the careers of new investigators in the field of behavioral research in cancer control. Grantee and mentor survey interviews collected information on grantee background, source and type of funding, and perceived impact of the small grants program. A grant reviewer analysis was also performed to determine the reviewer's expertise, NCI or NIH funding, and number of publications.

Fifty-four of 64 grant applicants were interviewed for the assessment. Fifty-nine percent were female, 93 percent had Ph.D. degrees, and 61 percent were affiliated with a university. Of those interviewed, 59 percent were classified as "junior investigators in the field of behavioral research and cancer control."

All of the respondents reported intent to apply for funds to support additional research in cancer control. After receiving the R03 grant, each grantee submitted, on average, two other grant applications. A total of 197 grant applications were reported. Seventy-five of these applications were for continued funding of their R03 research topic. Fifty-two applications were unrelated to the R03 topic, and 70 grant applications concerned non-NIH applications related to the R03 topic.

The majority of respondents reported that their R03 awards had a positive impact on their career in a variety of ways. Seventy percent said that the R03 encouraged them to engage in further Principal Investigator work. Seventy-two percent felt that the experience helped them increase the number of their publications. Of the 84 percent of grantees who had participated in meetings and presentations, 87 percent said their R03 Award increased the number of presentations they made. When asked about their relationships with other researchers, 83 percent said receipt of the grant encouraged or enhanced interactions with other researchers in the field. Overall, the perceived impact of the R03 grant program includes career development, building of confidence, increased networking, establishment of an early relationship with NCI, experience with grant writing, and an increased familiarity with the NIH grants process. The program also aids in the collection of pilot data and moves innovative research forward (grantees classified their research as novel and did not believe it would have been funded at an R21 level). The small grants program also encourages a multidisciplinary approach and allows researchers to share their interests with NCI.

The application process starts when potential applicants contact the program coordinator, who triages projects to the appropriate program officer. There is a mentor requirement for R03 grants. There is also a time incentive for submitting an R03 application, since the application receipt dates are typically 2 months behind the R01 application receipt dates. This permits a significant proportion of R03 applications to be funded shortly after the initial review.

The current success rate of the program is 34 percent; since its inception, the program has provided \$2.2 million in support of 203 grants. The success rate of the small grants program is similar to other funding mechanisms. For example, in 2007, NCI R01 applications had a success rate of 20.9 percent, NCI R21 applications had a success rate of 13.6 percent, and all NCI R03 applications had a success rate of 35.6 percent.

Overall, the program increases funding options for new and junior investigators and helps fulfill the NCI mission. Also, the R03 program fills a gap left by the discontinuation of the R29 mechanism. It also appears to benefit behavioral scientists by allowing them to conduct smaller studies. This small grants program is an ideal program for investigators who need to collect preliminary data for an R01 grant application. The Behavioral Research Program staff enjoys working with enthusiastic new scientists.

In conclusion, analysis indicates that the Behavioral Research Program small grants program provides significant impetus for new investigators to continue their research activities in the behavioral field. Without the R03 funding, grantees might not have been able to conduct and continue their research.

Key Points of Discussion—Session IV-6

- v Researchers should agree to participate on study section panels if asked. The peer-review process depends on high quality reviewers.

Concurrent Session IV-7: Community Grant-Writing Session

Moderator: Theresa J. Miller, Congressionally Directed Medical Research Programs (CDMRP), Department of Defense

Tips on Writing Grants for Community-Based Participatory Research

Gregg Talavera, San Diego State University

Community health centers provide health care to more than 16 million patients at an average cost of \$559 per patient. In San Diego, there are 33 fiscal entities. For a local study with a large sample size, the best approach is to use the Council of Community Clinics to help choose different clinics, though they are all fiscally independent.

University-community partnerships were formed between San Diego State University, the University of California, San Diego, and the San Ysidro Health Center (SYHC). SYHC has 52,000 registered patients at six different medical facilities, along with access to randomized clinical trials and service-oriented projects. These types of relationships and infrastructure-building are important. Infrastructure has helped elevate SYHC to a level of sophistication adequate to partner with a university and obtain more than one grant. A center for research with its own IRB was created within SYHC, which helped build infrastructure for CBPR. Additionally, the organization recommends cross-training staff to avoid having to recruit staff when new funding announcements are received.

SYHC has funding from federal agencies, private foundations, and university-community partnerships. SYHC performs work based on subcontracts; the University does science and writing and SYHC uses its labor force to access the community. Some SYHC staff members are being developed into young investigators so that they can build portfolios and get funding directly from NIH. The Council of Community Clinics received state and county funds for its programs, some of which are subcontracts with SYHC.

The selling point for a relationship with a community organization is the overlap of science and service. This benefits the individual patient, the clinic infrastructure, and the community that the organization serves. Research organizations can be established at community-based organizations.

Community Partnership and Participation: U.S. Department of Housing and Urban Development Strengthening Community Capacity Through Training, Outreach, and Collaboration

Carol Payne, U.S. Department of Housing and Urban Development

The mission of the Department of Housing and Urban Development (HUD) is to increase home ownership, support community development, and increase access to affordable housing free from discrimination. HUD's strategic goals include strengthening communities and promoting participation of grassroots faith- and community-based organizations.

The HUD Center for Faith-Based and Community Initiatives (CFBCI) cultivates support for grassroots faith- and community-based organizations (FBCOs) because these types of organizations strengthen the

communities of the United States. CFBCI strives to position FBCOs at the forefront of policy thinking and promotes a comprehensive approach to community and economic development. CFBCI conducts free 2-day training sessions to teach community groups how to develop and write grant proposals in order to help them access federal funding. In addition to grant writing, attendees learn about organizational development and models for evaluation of program effectiveness. These workshops also familiarize trainees with HUD grant programs and SuperNofa (Super Notice of Funding Available), which publicizes HUD's competitive grant programs.

HUD also has a checklist for starting a nonprofit called "Are you ready to be a 501(c)(3)?" The list addresses issues such as board development, strategic planning, program management, and financial management principles.

The HUD Policy Development and Research Office conducts research, testing, and demonstration projects related to the Department's mission and promotes university-community partnerships through grants and technical assistance. The Office houses the Office of University Partnerships, which supports a number of centers and programs, including the Doctoral Dissertation Research Center, the Community Development Work Study Program, Community Outreach Partnership Centers, and the Tribal Colleges and Universities Program. Community Planning and Development funds are given to cities to address local problems, which can include health issues. Summit participants should consider developing a relationship with community block programs in their cities. Helpful documents include "Community Connections: A User's Guide to HUD Programs" and "Empowering Local Communities Through Leadership Development and Capacity Building."

Leveraging Resources: Best Practices From a Community Partners Standpoint

Jackie Burton, Mississippi County Cancer Council

The Mississippi County Cancer Council (MCCC) was established in 2002 with a total of 12 members, all of who are community leaders such as judges, state representatives, physicians, cancer survivors, and other residents of Mississippi County. Community partners of MCCC include the Arkansas Cancer Community Network (AR-CCN), the Mississippi County Coalition for Tobacco Free Arkansas, and a number of other organizations. The mission of the Council is to reduce cancer health disparities and educate the community about cancer. The Council also provides free cancer screenings, supports cancer research, and conducts support groups.

Resources that the Council utilizes include local physicians, volunteer medical professionals, the American Cancer Society, a local sorority (which helped with AIDS testing), the local newspaper, and community navigation services. MCCC also leverages the resources of its community partners. For example, AR-CCN provides in-kind support and Arkansas Northeast College works with local school districts to provide cancer awareness education to students. MCCC also holds fundraisers such as a fish fry, chili cook-off, and Bike Ride for Cancer.

Funding Opportunities Through the Department of Defense Health Disparities Program

Theresa J. Miller, CDMRP, Department of Defense

Funds for the Congressionally Directed Medical Research Programs are added to the Department of Defense budget by Congress and Congressional guidance drives the establishment of CDMRP budget. Currently, there are programs for breast, prostate, and ovarian cancers. CDMRP grant applications are reviewed through a two-tiered process that includes consumer advocate representation. These awards do not follow the same scoring pattern that NIH and other entities use. These funds are used to support highly innovative research.

The CDMRP Minority and Underserved Population Program was established to address disparities in incidence, prevalence, and mortality rates of cancer and disease among underserved and underrepresented populations. Its mission is to enhance CDMRP's effort to address disease disparities by creating new funding opportunities, reaching out to the scientific community, and partnering with other agencies. The CDMRP Prostate Cancer Research Program offers both Health Disparity Research Awards and Health Disparity Training Awards, which fund research focused on resolving prostate cancer incidence and mortality disparities. The Research Awards are for investigators transitioning to their first independent faculty positions as well as early-career and established investigators. Training Awards are designed for M.D./Ph.D. investigators and postdoctoral fellows. Appropriate focus areas for these awards are race and ethnicity, socioeconomic status, access to care, insurance status, age, geographic area, and culture.

The Breast Cancer Research Program Historically Black Colleges and Universities (HBCU)/Minority Institutions (MI) Partnership Training Award was implemented to establish successful, independently funded breast cancer researchers at historically black colleges and universities. The program supports at least two faculty members at HBCU/MIs, allowing them to acquire training in breast cancer research. Training and research should lead to publications and independent breast cancer research funding. For this program, potential investigators must submit a pre-proposal, as proposal submission is by invitation only. Topics of special interest include disparities in underserved and minority populations, epidemiology (molecular, nutrition, diet, and environmental factors), access to care, treatment and outcomes, social and behavioral sciences, and public health and other population-based research.

CDMRP funding mechanisms include the Concept Award, the Idea Award, and the Synergistic Idea Award. The Concept Award funds the exploration of highly innovative new concepts to create avenues for investigation. It encourages the exploration of innovative, high-risk questions in breast cancer. No preliminary data are allowed in the proposals for this award, which provides \$75,000 plus indirect costs for 1 year (which can be extended). The Idea Award has the same intent as the Concept Award; innovation is the most important review criteria for proposals. Researchers at any level may submit proposals, and preliminary data are not required. This award provides \$375,000 for up to 3 years of breast or prostate cancer investigation, or \$650,000 for up to 5 years of breast cancer investigation. The Synergistic Idea Award funds collaborations between two investigators who address an innovative and high-risk but high-reward research question from synergistic and complementary perspectives. The most important review criteria are innovation and synergy, and no preliminary data are required. The investigators must be independent and faculty-level (or equivalent). For breast cancer, funding is for \$500,000 for up to 2 years or \$850,000 for up to 5 years. For prostate cancer, investigators can be given \$750,000 for up to three years.

To prepare for submission for these awards, investigators should read the PA or Broad Agency Announcement guidelines carefully, considering whether their intended proposal fits within the mission and goals of the agency. Guidelines should be followed *exactly*. Questions should be directed to relevant program personnel.

Key Points of Discussion—Session IV-7

- v Community-based organizations need to be sophisticated to ensure that partnerships with researchers are equitable. It is important to locate researchers who have the community's best interest in mind. Community-based organizations need to empower themselves. For example, they should insist on reviewing the budget before writing a letter of support for a grant application.

Wednesday, July 16, 2008

Plenary V—Science of Patient Navigation: Images From the Field

Moderator: Sheila Prindiville, Coordinating Center for Clinical Trials (CCCT), NCI

Defining the Science of Patient Navigation

Donald Dudley, The University of Texas Health Science Center at San Antonio

It is difficult to rigorously evaluate patient navigation and patient navigators because there are innumerable services and combinations of services that patient navigators can and do provide. One of the first tasks carried out by the nine sites funded through the NCI PNRP was to develop metrics to evaluate patient navigation. The diverse group of investigators met over the course of a year and a half to develop a minimum set of data elements that would be collected by all participating sites. These included primary outcome variables such as time from a positive screen to a definitive diagnosis; time from definitive diagnosis to therapy initiation; time from initial therapy start to finish; number of participants lost to follow-up; patient satisfaction; and cost effectiveness. An additional set of optimal data elements were also identified; these will be collected at some of the sites, allowing multisite analyses of secondary outcomes as well. Overall, more than 600 common data elements were developed and compiled into the program's data dictionary.

The common data elements include information about both patients and navigators. Information gathered on patients includes demographics, socioeconomic status, family history, and comorbidities. Data are collected regarding resources the patients have at their disposal and treatment-associated costs. Disease-specific information is also collected, including diagnostic work-ups, definitive diagnosis, stage of disease, treatment, participation in clinical trials, and eligibility for the patient navigation study. A number of different survey instruments are also administered to patients.

Information about the navigators is collected at each site. This includes demographic information, socioeconomic status, and information on the navigation activities they perform. The navigators fill out a tracking log that focuses on patient barriers and what has been done to help the patient address these barriers. Navigators are evaluated by other members of the scientific team, usually their supervisors; these assessments address client interaction, care management interventions, and documentation.

The nine PNRP sites are very heterogeneous with regard to the populations they serve and their healthcare delivery systems. These factors influence the types of studies the sites undertake. The UTHSCSA site, which focuses on breast and cervical cancers, was planning to conduct a randomized trial to study patient navigation, but system-wide reorganization prevented this. Instead, the group has used a convenience sample approach. Each UTHSCSA navigator was paired with a *promotora*, which is a culturally savvy lay community health worker. Many of the *promotora* participating in the San Antonio patient navigation program are health professionals from Mexico. The navigators focus on functional/organization barriers and funding issues while the *promotora* deal with cultural and social barriers, help patients arrange transportation, and track patients.

The UTHSCSA patient navigation program interfaces with many community health centers, many of which have never been involved in research projects. Many of the centers go through a process similar to the grief process described by Elizabeth Kubler Ross (i.e., denial, anger, bargaining, depression, and acceptance). The centers start out by ignoring the study, then express anger about having to spend time working on it. This leads to bargaining (e.g., "I guess I can help as long as I don't have to fill out any forms") and grudging acceptance. Finally, most of staff eventually become enthusiastic participants, excited about helping patients obtain navigation services because they recognize that it helps them do

their job and is valuable for the patient. Dr. Dudley developed a system of interacting with the community health center staff to help ease this process; he calls it the “P’s of Overcoming Stages of Research Grief.” The components include patience, pampering, pleasantness, passion, performing, praise, process, protection, and persistence. These principles help the research team build a healthy and productive working relationship with community health center staff.

Operationalizing Patient Navigation: Making it Happen in the Community

Elizabeth Calhoun, University of Illinois at Chicago

As part of the cooperative group experience, instruments such as a patient navigator tracking log and performance checklist were developed to collect data elements for the evaluation of patient navigators.

The patient navigator tracking log links patient barriers with the type and level of services that are necessary to overcome them. Patient-level barriers that were identified include transportation, housing, lack of social/practical support, low literacy levels, employment/financial problems, disabilities, comorbidities, and negative attitudes toward providers. Many patients also experience cultural barriers, which may include language barriers, fear, and particular perceptions/beliefs about health and healthcare. Other barriers attributed to the healthcare system include inadequate communication with medical personnel, inconvenient locations of health facilities, problems with scheduling care, and insurance issues. The tracking log also links barriers with an accompanying action; any time the navigator accompanies a patient to a health service, social service, or any other service, it is captured in the log.

The patient navigator performance checklist documents the quality of interaction of navigators with their patients. Some examples of quality indicators included on the checklist are ability to establish rapport, monitoring clients’ understanding, assessing/reassessing patients’ needs, appropriately identifying barriers to care, providing patients with appropriate information, assisting patients in accessing resources, assuring quality and accuracy of data collection, and assuring the confidentiality of client data.

A number of patient satisfaction measures have also been developed to evaluate patients’ satisfaction with their navigators and care. These measures help collect patients’ perceptions about how their navigators help them access care and if/how this influences patients’ perceptions of the care they receive.

A PNRP substudy has been initiated to qualitatively analyze patient navigators. This study involves observing navigators and documenting the tasks they perform. Navigator activities are carried out in at least five areas: navigation, facilitation, maintaining systems, documentation, and tasks not directly related to their navigator role. Navigation activities involve working *with* patients and include tasks such as explaining medical procedures, asking about barriers, exploring concerns, providing emotional support, and coaching patients to more effectively communicate with their healthcare providers. Facilitation activities are those that involved working *on behalf of* patients; these include coordinating medical care team communication, integrating information, and enlisting other providers to address patients’ fears/needs. Navigators maintain systems by identifying patients who might benefit from navigation, networking/interfaces with clinicians, and reviewing cases. Navigators spend significant time documenting their work; in addition to recording the steps they take to help their patients, they also enter patient data into databases and record other information/activities. Activities not directly related to navigating include research-related activities, providing clinical back-up, and interacting with co-workers.

Among other things, this study reveals that contextual factors are important to the work of patient navigators. For example, a new patient will require different services than an established patient. Support will differ depending on whether the patient is in the diagnostic resolution phase or actively receiving treatment. Organizational factors also make a difference.

Navigation at Work: Boston

Wanda Turner, Boston Medical Center

Patients at the Boston University Medical Center are from diverse ethnic backgrounds and inner city communities. The focus of the patient navigation program is breast cancer. Experiences such as domestic violence, high poverty levels, being uninsured, coming from single-income households, and living in high-crime neighborhoods often inhibit women from receiving annual mammograms and from making medical appointments a top priority. The following three case examples demonstrate how navigators work on behalf of the patient, the detective work involved, and the difficulties in locating patients and addressing barriers to care.

The first case exemplifies how a navigator interacts with a patient in the community and the importance of community connections. A 45-year-old African-American twin with a family history of breast cancer and a previous history of substance abuse presented with an abnormal mammogram; the breast core biopsy results were positive for breast cancer. This was a known patient from the community and Ms. Turner, the assigned patient navigator, worked to enroll her in the navigation program. Ms. Turner scheduled prompt appointments, accompanied her to find out results, and educated and empowered her to make decisions concerning follow-up and treatment plans. This patient underwent breast surgery and is now receiving radiation treatments. Ms. Turner referred her to many resources through the American Cancer Society, and the patient now advocates for her own medical care and educates others.

The second case required much detective work regarding a 30-year-old African-American woman referred to the breast clinic for an abnormal clinical breast exam. The patient insisted she had a breast ultrasound at her community health clinic, but the ultrasound films could not be located. The patient assumed the clinical breast exam was a breast ultrasound; the detective work revealed the patient's misconception and presented an excellent opportunity to educate her about breast health. It also helped the patient receive an ultrasound in a more timely manner.

In the last case, a patient received results of a BIRAD 5 from a screening mammogram, but over a 2-month period Ms. Turner was unable to contact her by phone or letter to discuss her results. Knowing the community, she conducted a home visit to discuss abnormal results and need for follow-up. The discussion made it clear that the patient had many barriers, such as family, money, and housing issues, in addition to a greater concern for her HIV (human immunodeficiency virus) infection status. Despite making multiple follow-up appointments over a 3-month period, this patient chose not to come back. While Ms. Turner was unable to get the patient in for care, she was successful in educating her about breast disease and the consequences of not following up on her abnormal results.

Documentation is very important in patient navigation. Information about barriers to care, patient concerns, contact with patients, and actions taken to help the patient can be documented in an electronic medical record. These records help keep doctors informed about their patients' issues and concerns and act as a source of study data.

Ms. Turner offered a number of "lessons learned." Navigation involves a lot of "detective work" to successfully connect with patients, locate films and other information, and manage appointments. High-risk patients generally require more time; home visits are sometimes necessary, and these patients often require more education and medical follow-up. It is important to form relationships with clinical support staff and also to actively engage physicians in order to obtain information that should be passed on to patients. Finally, navigators need to know their boundaries; it is not their role to provide patients with test results or information in addition to that provided by the patients' physicians. The navigator's job is to make sure the patient understands information and test results that come from the physician and arrange a navigation plan to ensure that the intervention plan outlined by the physician is carried out.

Navigation at Work: Washington, DC

Diana Garcia, Washington Hospital Center

The Preventorium is a clinic at Washington Hospital Center founded by Dr. Elmer Huerta in 1994. Primarily serving the low-income and uninsured Latino community, the clinic has seen almost 25,000 patients so far. The particular problems that Latino women face when seeking medical care include cultural, language, transportation, and financial barriers; poverty and lack of medical insurance; limited access to programs; and a fragmented health care system.

The navigators' responsibilities at the Preventorium are to follow patients from the time they are given a mammogram order to resolution of their case. Navigators connect patients to different screening programs, coordinate services and follow-up, and help to bring cancer prevention programs into the community. Since the Preventorium became part of the PNRP in July 2007, 1,758 patients have been seen. Mammograms were ordered for 765 women, with 198 diagnosed as abnormal. To date, 60 women have been recruited to the patient navigation program.

It is important to remember several things when integrating patient navigators into an existing institution. Everyone in the clinic needs to work together to ensure that follow-up appointments are scheduled, screening mammograms performed, and results delivered to patients in a timely manner. It is also important to hire a bilingual, bicultural navigator who is able to effectively interact with patients. Lastly, it is crucial to stay in contact with patients, using telephone, e-mail, and/or personal letters.

A Patient's Story

Norma Davila

Ms. Norma Davila shared her experience as a cancer patient at the Washington Hospital Center. Ms. Davila met Diana Garcia, her navigator, the day Dr. Huerta found a breast tumor and requested a mammogram and sonogram. Ms. Garcia's words of support, "together, we will make it," became the beginning of Ms. Davila's recovery.

Ms. Davila's mammogram results required a biopsy. However, even though she is a legal resident of the U.S., her low income and lack of health insurance were major barriers to her receiving care. Ms. Garcia directed her to the clinical center of the National Institutes of Health, where patients are studied and treated. The biopsy results showed stage IIB cancer in the right breast, but the clinical center did not have an oncologist so Ms. Davila had to search for yet another medical center. Ms. Garcia guided her to the Inova Fairfax Hospital in Virginia, which receives help from the Avon Foundation. Ms. Davila received eight chemotherapy sessions and is eternally grateful for the help of her patient navigator. She now wants to give back by speaking in public. Patient navigator programs make it possible for many women like Ms. Davila, who lacked guidance and information, to have hope of being saved from cancer.

Key Points of Discussion—Plenary V

- ✓ The term "patient navigator" often does not translate well into other languages. Bilingual navigators should explain their role in terms of words of support and encouragement. However, it is important to maintain boundaries in these cases, because patients can become emotionally attached when they do not speak English.
- ✓ The frontiers of research in patient navigation will be to define what elements of navigation actually work, focus on those concepts, and determine how to expand those concepts on a global scale.
- ✓ It is a difficult task to balance quality and improvement in care with the actual cost of that care when it comes to determining the cost-effectiveness of patient navigator programs.

Plenary VI—Bringing It All Together: Concept to Clinic to Community

Moderator: LeeAnn Bailey, Diversity Training Branch, Center to Reduce Cancer Health Disparities, NCI

Genomic Profiling of Early-Onset Breast Cancer in African-American and European-American Women

Tyesha Farmer, University of Alabama at Birmingham

European-American women have a higher incidence of breast cancer than women of other ethnic backgrounds; however, African-American women have a slightly higher incidence of early-onset breast cancer. Breast cancer in this population is more aggressive and, consequently, African-American women have higher mortality rates and lower survival rates. A number of factors contribute to breast cancer disparities, such as screening practices, socioeconomic status, and environmental factors. However, even when controls for these confounders are used, disparities between African-American and European-American women persist.

Biological differences in breast tumors have also been reported. African-American women have a disproportionately higher frequency of grade III breast tumors compared with women of European descent. Also, African-American women's breast tumors are more likely to be of the basal, triple-negative subtype compared with European-American women's tumors, which are more likely to be luminal A—the least aggressive breast cancer subtype. The current study used array-based comparative genomic hybridization—a whole genome analysis designed to identify gains and deletions of genetic material—to determine whether the differences in tumor phenotype observed between African-American and European-American early-onset (age ≤ 50 years) breast cancer correlate with specific patterns of genomic aberrations that represent different pathways of breast cancer development.

In the data set (50 matched pairs of samples), higher grade, aggressive subtype breast tumors were observed more often in the African-American population in comparison with the European-American population; a trend consistent with previously published literature. Both African-American and European-American women's breast tumors exhibit complex genome copy number alterations, and several loci were identified that were differentially altered between the breast tumors of the two ethnic groups.

Future studies will explore the ancestry of the identified amplifications and deletions to determine whether there are African or European alleles that are segregating with these particular aberrations. Understanding the genetic drivers of early-onset breast cancer in African-American women may uncover novel therapeutic targets for breast cancer.

Gene Expression Profiling Reveals Tumor Immunobiological Differences

Tiffany Wallace, Center for Cancer Research, NCI

Prostate cancer disproportionately affects African-American men in terms of incidence, mortality, and morbidity; their incidence rate is 60 percent higher compared with European-American men and the mortality rate is doubled compared with all other ethnic groups. Socioeconomic factors do not fully explain the differences in prostate cancer incidence, aggressiveness, and mortality among different ethnic groups. Gene profiling experiments have been conducted to identify biological and genetic differences that might contribute to this finding.

The experiments compared tumors from African-American men with tumors from European-American men and then attempted to identify specific genes and biological pathways that could be responsible for the apparent disparities in prostate cancer. Dr. Wallace's team looked at 69 primary prostate tumors—33 from African-American men and 36 from European-American men—and investigated non-tumor tissues from the surrounding prostate of 18 of the recruited patients. When comparing the African-American

tumors with the European-American tumors, 162 genes were differentially expressed; 134 were found to be higher expressed in African-American tumors, while the remaining 28 were lower expressed.

A pathway analysis was then conducted to investigate genes differentially expressed by ethnicity. Pathway analysis is a bioinformatics tool that groups genes with similar functions into specific pathways and biological networks. After comparing the tumors from the two ethnic groups, it was discovered that the differentially expressed genes were enriched in various immune and inflammatory-related pathways. These pathways were not evident in the non-tumor tissues.

The next step was to identify the specific genes playing a role in these immune and inflammatory pathways. One such gene is indoleamine-2,3-dioxygenase (IDO), which when overexpressed is correlated with poor prognosis in numerous cancer types. IDO induces its immunosuppressive effects by degrading tryptophan, thus leading to events such as T-cell inhibition and regulatory T-cell induction. Tumors from African-American men showed a higher expression of IDO when compared with European-American patients, as well as higher expression of interferon gamma—the causative agent for upregulating IDO. These differences may have important consequences in disease aggressiveness and response to therapy, especially in the African-American population.

Advancing Cancer Research Through Biospecimen Science

Carolyn Compton, Office of the Director, NCI

Biospecimens are a powerful key to addressing the issue of cancer disparities. All patients are biologically different and consequently 30 percent of all cancer sufferers do not benefit from any of the medicines that are currently available for cancer treatment. However, there is a new horizon for cancer treatment. New molecular technologies now available allow scientists to classify cancers based on their molecular makeup.

Instead of using generic therapeutic treatments, treatment will be tailored to fit the molecular characteristics of a particular tumor while also considering the patient's individual molecular background. In the transition to these targeted therapies, scientists are completely dependent on patients to provide fuel for such innovative research. NCI's Office of Biorepositories and Biospecimen Research is the starting point for the collection of high-quality tissue specimens, which are then banked and provided to researchers to uncover the molecular data needed for new, personalized diagnostic and therapeutic agents.

However, there is currently a lack of standardization and therefore a lack of high-quality biospecimens—this is the most significant roadblock for translational research. Incorrect immunostaining, for example, can lead to incorrect diagnosis and treatment. A lack of participation by minority populations is another hindrance to translational research; this creates an unequal representation of biospecimen collections to fuel studies, which in turn hinders development of new molecular therapies that are effective for all populations.

There are cultural, ethical, legal, and policy implications of human tissue handling for research. During the patient consent process, researchers should ask participants about cultural issues regarding the biospecimen, including religious, cultural, or personal restrictions, wishes for family to have access to biospecimens, and instructions for disposal or return of specimens. Researchers need to respect the beliefs of communities but also educate on the importance of biospecimens to clinical care and research.

Genomics of Cancer Health Disparities: A Novel Partnership Model

Steven Patierno and Norman Lee, The George Washington Cancer Institute, and Georgia Dunston, Howard University

Washington, DC, has some of the highest cancer mortality rates in the country, a large minority population, and extensive healthcare barriers; all of these factors lead to severe cancer disparities. To address this problem, geographic maps are used to track cancer by neighborhood to determine where “hot

spots” are and where more resources need to be applied. In addition, a number of collaborations and partnerships have been established to integrate community needs (e.g., education and outreach, cultural sensitivity, screening for early detection, and clinical care for all) with research and public policy.

One such partnership for prostate cancer outreach—the Community-by-Community Cancer Control Program—includes the NCI, American Cancer Society, local TV and radio stations, Safeway, the Men’s Health Network, Amgen, and the NCI Clinical Trial Information Service. A number of community wellness initiatives have been launched through this program; in the course of 18 months, over 1,200 face-to-face contacts with DC minority population residents were made. Other screening programs, such as “Get in the Game” and “Don’t Forget,” have prompted many men to participate in free screenings—a total of 3,000 men for both PSA and DRE over a 22-month period.

To address the genomics of cancer disparities, a collaboration was established between the GW Cancer Institute, the Genomics Center at GW, the J. Craig Ventor Institute, Howard University Cancer Center, the National Human Genome Center at Howard University, NCI, and CRCHD. The challenge of this program is to translate knowledge gained from the Human Genome Project to the study of tumor biology and ultimately the elimination of health disparities. This collaboration hopes to maximize information content; acquire mRNA and microRNA expression data, SNP information, copy number variation information, DNA methylation patterns, and gene mutations for each clinical specimen. This genomic data can then be integrated for a systems approach to study gene regulatory networks and integrated pathways. Lastly, this data can be used to determine whether there are recurrent networks or connections specific to one population versus another population.

Studies show that there is a relationship between the history of populations, their adaptation to their environments, the expression of particular alleles, and the biological mechanisms involved in the processes of disease. The specific research objective is to use population differences in human genome variation (i.e., ancestral information markers) as a probe in the development of an immunogenomics strategy for dissecting the biology of prostate cancer in African-American men. The challenge will be using the genome to redefine concepts of race (i.e., individual and group identity) in health and disease and to push biomedical science toward personalized medicine. Genome variation information can be used to personalize population risk and to identify environment-dependent phenotypic variation in complex diseases.

Key Points of Discussion—Plenary VI

- ✓ The goal of using genomic information to address cancer health disparities is to map phenotypic differences onto genetic markers and determine what pathways these genes fit into and how the pathways relate to disease. Social ideas of “race” are not sufficient to address the biology involved in cancer health disparities.
- ✓ The high incidence of HIV and HPV, as well as smoking and alcohol abuse, contribute to disproportionately high incidence rates of oral cancer in the metropolitan DC area. This epidemic and its viral causative are being tracked very closely.

Closing Remarks—Summit 08 Planning Committee Chairs

Belinda Locke, Leslie C. Cooper, Tarsha McCrae, CRCHD

Ms. Locke thanked meeting attendees for their enthusiastic participation in the meeting. She noted that the numerous presentations highlighted the dedication of the research community and CRCHD to eliminating cancer health disparities. She reminded participants of the programmatic meetings and both she and Dr. Cooper encouraged people to attend the mock review session.

Ms. McCrae asked meeting participants to use the information gathered through the Summit to strengthen their programs, work on next steps, and look for additional funding opportunities. She also encouraged

researchers who had not yet been funded to continue to conceptualize their ideas and work with CRCHD to develop grant applications.

CRCHD and other NCI staff, NOVA Research Company, CRCHD grantees, and other Summit attendees were thanked for organizing and contributing to Summit 08. Ms. McCrae encouraged the audience members to access the Summit 07 report on the CRCHD Web site and look for the Summit 08 report there in the future.

Appendix A: Glossary of Acronyms and Abbreviations

<u>Acronym</u>	<u>Definition</u>
2DG	2-deoxyglucose
AACR	American Association for Cancer Research
AANCART	Asian American Network for Cancer Awareness, Research, and Training
ABC	Aneurismal bone cysts
ACS	American Cancer Society
AML	Acute myeloid leukemia
APL	Acute promyelocytic leukemia
AR-CCN	Arkansas Cancer Community Network
ATECAR	Asian Tobacco Education, Cancer Awareness, and Research
ATO	Arsenic trioxide
ATRA	All trans-retinoic acid
BET	Black Entertainment Television
BMC	Boston Medical Center
BMI	Body mass index
BRD	Bromodomain
BSA	Board of Scientific Advisors
CAM	Complementary and Alternative Medicine
CBP	CREB binding protein
CBPR	Community-Based Participatory Research
CCOP	Community Clinical Oncology Program
CDC	Centers for Disease Control and Prevention
CDMRP	Congressionally Directed Medical Research Programs
CES-D	Center for Epidemiologic Studies Depression Scale
CFBCI	Center for Faith-Based and Community Initiatives
CIS	Cancer Information Service
CLAS-ACT	Culturally and Linguistically Appropriate Services And Clinical Trials
CMS	Centers for Medicare and Medicaid Services
CNP	Community Networks Program
CRC	Colorectal cancer
CRCHD	Center to Reduce Cancer Health Disparities
CREST	Cancer Research Experience and Student Training
CRF	Cancer-related fatigue

CSO	PECaD Clinical Studies Outreach Program
CSR	Center for Scientific Review
CURE	Continuing Umbrella of Research Experiences
DCB	Division of Cancer Biology
DPMS	Mannosylphospho dolichol synthase
DRE	Digital rectal examination
EDICT	Eliminating Disparities in Clinical Trials
EMR	Electronic medical record
ETS	Environmental tobacco smoke
FBCO	Faith- and community-based organizations
FFQ	Food Frequency Questionnaire
GAO	Grant Administrative Officer
GIS	Geographic Information Systems
GMaP	Geographical Management of Cancer and Cancer Health Disparities Programs
HBCU	Historically Black Colleges and Universities
HHS	United States Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HRSA	Health Resources and Services Administration
HUD	Department of Housing and Urban Development
IC	NIH Institutes and Centers
IDO	Indoleamine-2,3-dioxygenase
IRB	Institutional review board
IRG	Initial Review Group
LEP	Limited English Proficient
LLO	Lipid-linked oligosaccharides
LOI	Loss of imprinting
LPrA	Leptin peptide receptor antagonists
MassCONNECT	Massachusetts Community Networks to Eliminate Cancer Disparities through Education, Research, and Training
MBCCOP	Minority-Based Community Clinical Oncology Program
MCCC	Mississippi County Cancer Council
MI	Minority institution
MI/CCP	Minority Institution/Cancer Center Partnership Program

MMC	Meharry Medical College
MSI	Minority-serving institution
NACRP	Native American Cancer Research Partnership
NAU	Northern Arizona University
NAU	Northern Arizona University
NBCCEDP	National Breast and Cervical Cancer Early Detection Program
NCI	National Cancer Institute
NIH	National Institutes of Health
NRSA	National Research Service Award
OB-R	Leptin receptor
OTH	Oklahoma Tobacco Helpline
P2P	Pipeline to Partnerships
PA	program announcement
PD	Program Director
PECaD	Program for the Elimination of Cancer Disparities
PN	Patient navigator
PNRP	Patient Navigation Research Program
PP1	Protein phosphatase 1
PRQ	Puerto Rico Quitline
Prx	Peroxiredoxin
PSA	Prostate-specific antigen
PSA	Public service announcement
RA	Retinoic acid
REALM	Rapid Estimate of Adult Literacy in Medicine
RFA	Request for Applications
RFP	Request for Proposals
RT-PCR	Reverse transcriptase polymerase chain reaction
SAICN	Southwest American Indian Collaborative Network
SBIR	Small Business Innovation Research program
SCLD	State Cancer Legislative Database
SEER	Surveillance, Epidemiology, and End Results program
sLeX	Sialyl Lewis X
SNP	Single nucleotide polymorphism
SPORE	Specialized Program of Research Excellence
SREP	Summer Research Enhancement Program

SRG	Scientific Review Groups
SRO	Scientific Review Officer
SST2	Somatostatin receptor
STTR	Small Business Technology Transfer program
SuperNofa	Super Notice of Funding Available
SURF	Summer Undergraduate Research Fellowship
SYHC	San Ysidro Health Center
UA	University of Arizona
UAB	University of Alabama
UTEP	University of Texas, El Paso
UTHSCSA	University of Texas Health Science Center San Antonio
VA	Veterans Affairs
VEGF	Vascular endothelial growth factor
WINCKABB	Weaving Islander Network Cancer Knowledge, Attitude, Beliefs, and Behaviors
