

Linkage

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Diesel Exhaust Exposure in Miners Linked to Lung Cancer

After 20 years of research, results from the landmark Diesel Exhaust in Miners Study were published in March in the *Journal of the National Cancer Institute*. Findings from two complementary papers, a cohort mortality study and a nested case-control study of lung cancer, provide evidence that exposure to diesel exhaust may cause lung cancer in humans. This is the first report of a significant exposure-response relationship for diesel exposure and lung cancer based on quantitative estimates of historical diesel exposure with adjustment for smoking and other potential confounders. The collaborative effort between NCI and the National Institute for Occupational Safety and Health (NIOSH) was led by **Debra T. Silverman, Sc.D.**, Chief of the Occupational and Environmental Epidemiology Branch (OEEB), and Dr. Michael Attfield, formerly of NIOSH.

Why Study Diesel Exhaust?

Researchers first raised the possibility that diesel exhaust might cause cancer in humans in 1955, after discovering components of diesel exhaust that were known to cause tumors in experimental animals. In 1989, the International Agency for Research on Cancer (IARC) classified diesel exhaust as a “probable” carcinogen based primarily on data from animal studies; data from humans were considered too limited to establish causality. Occupational exposure to diesel exhaust is common among certain groups, including miners, mechanics, transportation workers, and other operators of diesel-powered equipment. Exposure is not limited to workers, however; diesel exhaust is ubiquitous in cities, and people who live near highways, ports, and rail yards may have considerable exposure to diesel exhaust throughout their lives.



Debra Silverman with the recruitment poster for the Diesel Exhaust in Miners Study.

DCEG Linkage

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A roof bolter machine, one type of diesel-powered equipment that is used in mines.

Since the 1980s, more than 35 studies have examined the relationship between lung cancer risk and diesel exhaust. Although most of these studies suggested a modest association between diesel exhaust exposure and lung cancer, few quantified exposure levels or adjusted for smoking in their analyses. These limitations of previous studies led Dr. Silverman and her colleagues to conclude that a need existed for further research on the carcinogenicity of diesel exhaust.

“It was vitally important to undertake a large study of diesel exhaust and lung cancer based on a quantitative assessment of historical exposure, taking into account smoking and other potentially relevant factors in order to estimate lung cancer risk,” Dr. Silverman said.

A Landmark Study

The Diesel Exhaust in Miners Study included four components: (1) an exposure monitoring study conducted from 1998 to 2001 (led by NIOSH), (2) a retrospective exposure assessment (led by NCI), (3) a retrospective cohort mortality study of 12,315 workers at eight non-metal mines (led by NIOSH), and (4) a nested case-control study of lung cancer deaths in the cohort (led by NCI). The researchers chose to

investigate exposure to diesel exhaust in underground mines because high levels of diesel exhaust from heavy equipment build up in the enclosed underground mining environment. Non-metal mines (i.e., mines that produce limestone, potash, salt, and trona) were selected to avoid confounding exposures to other potential carcinogens, such as radon.

The researchers characterized current and historical exposures to diesel exhaust, represented by respirable elemental carbon, and estimated personal exposures for each worker in the cohort. They based their estimates on thousands of measurements from exposure surveys at each mining facility, past Mine Safety and Health Administration enforcement surveys, and information from company records and interviews with long-term workers. In addition, the researchers reviewed records of inventories of working diesel equipment at each mine and ventilation data over time. The exposure assessment process is described in five papers published in the *Annals of Occupational Hygiene* (October 2010 and March 2012).

In the case-control study, the researchers interviewed subjects or next of kin about smoking behavior and other lung cancer risk factors, such as employment in other high-risk occupations and history of

nonmalignant respiratory disease. Several DCEG scientists assisted with the case-control study. **Jay H. Lubin, Ph.D.**, senior investigator (now retired) in the Biostatistics Branch (BB), conducted the continuous modeling of exposure data; **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, senior investigator in OEEB, collaborated on the analysis and mechanistic interpretations of the smoking-diesel interaction; **CDR Claudine M. Samanic, Ph.D.** (OEEB), assisted with the data collection and conduct of the study; and **Sholom Wacholder, Ph.D.**, senior investigator in BB, contributed to the case-control design and analysis. In addition, **Aaron E. Blair, Ph.D., M.P.H.**, a scientist emeritus of OEEB, offered general study guidance.

Diesel Exhaust and Lung Cancer

The cohort study, under the direction of Dr. Attfield, found that the risk of lung cancer among heavily exposed underground workers was five times the risk among workers in the lowest exposure category.

The case-control study, which was led by Dr. Silverman, confirmed the lung cancer findings from the cohort study and had the added strength of smoking histories. After taking smoking and other risk factors into account, the researchers found a threefold risk of lung cancer overall and about a fivefold risk among heavily exposed underground workers. The researchers estimated risk for several exposure metrics, with cumulative diesel exhaust exposure lagged 15 years yielding the strongest gradient in lung cancer risk.

For never smokers and light-to-moderate smokers, the risk of lung cancer death increased with more diesel exhaust exposure. Non-smokers with the highest level of diesel exposure were

seven times more likely to die from lung cancer than non-smokers in the lowest exposure category. In contrast, among miners who were heavy smokers, the risk of lung cancer death decreased with increasing levels of exposure.

“Despite the many challenges throughout the duration of this study, I’m proud to say that we persevered and finally published our findings.”

“Little is known about the interaction of smoking with diesel exhaust,” Dr. Silverman said. “The qualitative interaction we observed has not been reported previously and will require replication.”

The researchers offered possible explanations for the tapering off of risk at high levels of diesel exhaust exposure. Heavy smokers might be more likely to clear diesel exhaust particulate matter from their lungs than non-smokers, a phenomenon that has been reported previously among coal miners who smoke. Carcinogens in diesel exhaust and cigarette smoke also might operate along the same metabolic pathway in the body, competing with each other and saturating the pathway and, thus, diminishing the effects of both components.

Study Challenges and Impact

The Diesel Exhaust in Miners Study has been described as groundbreaking—not only because of its contribution to science but also because of the scientific and other challenges that the researchers overcame during the 20-year study period. For example, the careful exposure assessment and sophisticated methods development took years. “This study represents an enormous team

effort,” Dr. Silverman said. “Many people provided invaluable input during the different stages of the study.”

From the very beginning, the study had high visibility because of its potential impact on regulatory policy, which led to significant legal and political challenges. As early as the mid-1990s, the researchers faced delays resulting from lawsuits from a coalition of companies representing mining industry interests.

“Despite the many challenges throughout the duration of this study, I’m proud to say that we persevered and finally published our findings,” Dr. Silverman said.

Although the researchers studied miners with very high levels of exposure to diesel exhaust, the results may be applicable to other workers with similar levels of diesel exposure and may extend to people living in urban areas with high diesel exhaust levels. Environmental exposures to average respirable elemental carbon levels in the range of 2 to 6 $\mu\text{g}/\text{m}^3$ over a lifetime, as is typical in some highly polluted cities, are similar to the cumulative exposures experienced by the underground miners with the lowest exposures in the study. Even underground workers with low exposure levels experienced about a 50 percent increase in lung cancer risk.

The publication of the study results was timely because it preceded reviews by IARC and the NIH National Toxicology Program to reassess the health risks associated with diesel exhaust exposure. In June, IARC announced that it had reclassified diesel exhaust as a Group 1 human carcinogen, a category that IARC uses when sufficient evidence is available indicating that a substance is carcinogenic to humans. The NIH National Toxicology Program will hold a review of diesel exhaust later in 2012. ■

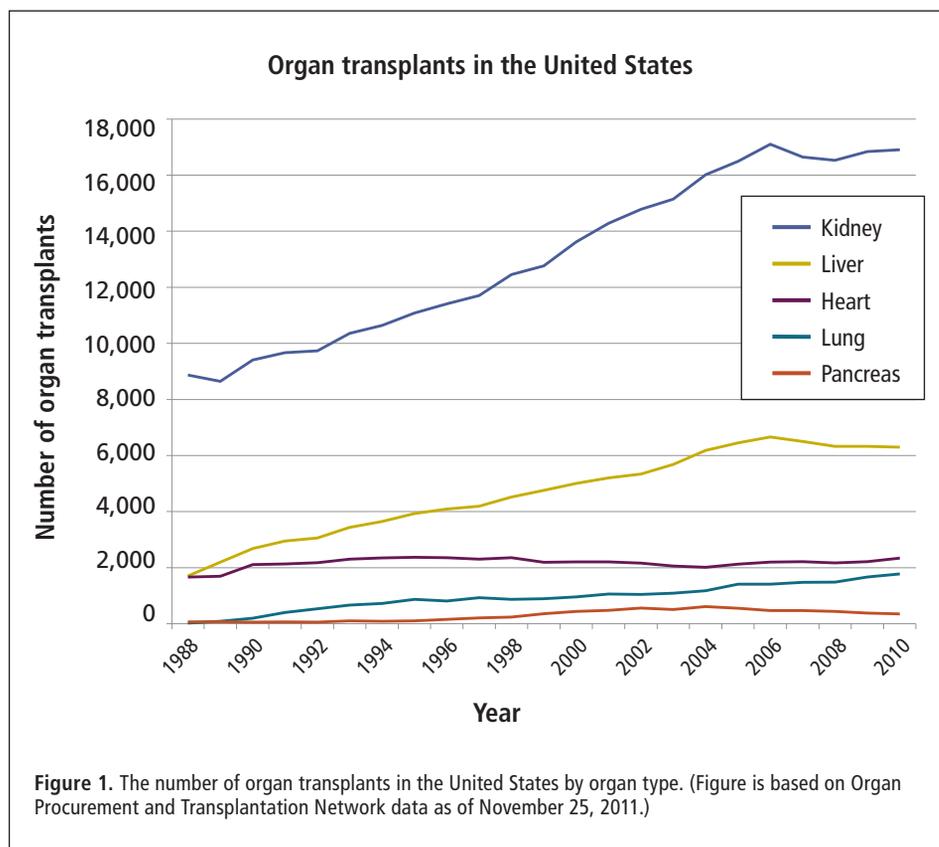
—Victoria A. Fisher, M.P.H.

CANCER RISK AMONG IMMUNOSUPPRESSED POPULATIONS

Since the influence of the HIV epidemic on cancer was first observed in the 1980s, investigators in the Infections and Immunoepidemiology Branch (IIB) have examined how oncogenic viruses and other opportunistic infections affect individuals with compromised immune systems. Today, DCEG's research portfolio on cancer among immunocompromised patients involves two distinct, yet related, study populations: (1) organ transplant recipients and (2) HIV-infected individuals and persons with AIDS. Organ transplants have increased in recent decades for certain organ types (see Figure 1), and recipients must take immunosuppressive drugs for the remainder of their lives to prevent organ rejection. Both groups provide valuable populations in which to study the interconnected roles of infections, environmental exposures, inflammation, and the immune response in the development of cancer. DCEG senior investigator **Eric A. Engels, M.D., M.P.H.** (IIB), leads the Transplant Cancer Match (TCM) Study and the HIV/AIDS Cancer Match (HACM) Study, two large and complementary registry linkage studies on cancer among immunosuppressed populations.

Transplant-related Immunosuppression and Cancer

More than five years ago, Dr. Engels met with officials from the Health Resources and Services Administration (HRSA), the Department of Health and Human Services agency that oversees the U.S. organ transplant program, to discuss the creation of a resource linking the U.S. transplant registry with multiple cancer registries. "It was an exciting opportunity to take an unprecedented look at



the cancer burden among solid organ transplant recipients," Dr. Engels noted, "but it was also daunting because of the logistics involved in getting all the approvals from the cancer registries." It took six years to get the study off the ground, but the efforts were well worth the time. The TCM Study now combines data from HRSA's Organ Procurement and Transplantation Network and 15 population-based state or regional cancer registries, making it the largest study of its kind.

Dr. Engels and other TCM Study researchers published the study's first article, which provides the most comprehensive description to date of the cancer burden among solid organ transplant recipients, in the November 2011 issue of the *Journal of the American Medical*

Association. The authors assessed linked registry data from 175,732 solid organ transplant recipients, who represented roughly 40 percent of the U.S. transplant recipient population between 1987 and 2008, and measured the risk of individual cancer types among recipients of all types of organs. The researchers found a twofold increased risk of cancer among transplant recipients. This finding confirmed results from earlier, smaller studies, but the large size of the TCM Study also allowed the investigators to evaluate the risk of rare cancer types.

"We were surprised to find that this population is at increased risk for a large number of different cancers—32 different types of cancer, including some that we don't commonly associate

with HIV and immunosuppression,” Dr. Engels noted. For example, the four most common cancers among transplant recipients and that occur more commonly in these individuals than in the general population were non-Hodgkin lymphoma (NHL) and cancers of the lung, kidney, and liver. NHL also is common among HIV-infected individuals and is associated with immunosuppression and Epstein-Barr virus, whereas liver cancer is associated with hepatitis B and C. However, researchers do not generally believe that lung and kidney cancers are associated with infection.

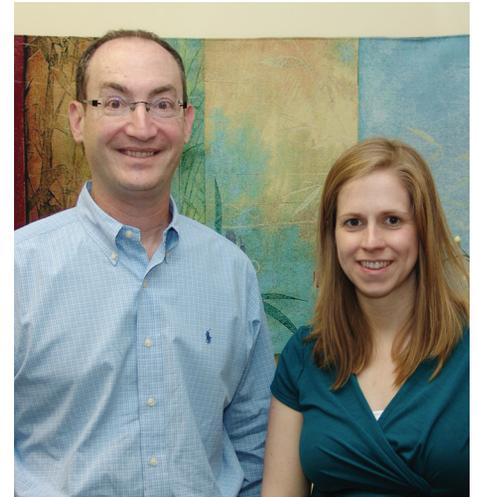
Having such a large, valuable resource as the TCM Study also permits swift follow-up studies on interesting leads. For example, **Todd M. Gibson, Ph.D.**, a postdoctoral fellow, and **Lindsay M. Morton, Ph.D.**, an investigator, both in the Radiation Epidemiology Branch, conducted an analysis of diffuse large B-cell lymphoma, a common and highly aggressive form of NHL. They observed an almost 14-fold elevation in the risk of this NHL subtype among transplant recipients compared with the general population. Dr. Gibson recently presented the findings of this study at the 2012 Annual Meeting of the American Association for Cancer Research.

Dr. Engels and his team plan to pursue these leads in order to characterize the proportion of cancers related to infection and impaired immune response as well as to shed light on other possible mechanisms, especially for cancers not linked to infection.

HIV and Cancer

DCEG’s HACM Study is an example of a unique resource that has permitted the examination of cancer trends among the HIV and AIDS population over time. **James J. Goedert, M.D.** (IIB),

and Dr. Robert Biggar (formerly of DCEG) initiated the HACM Study in 1990. The study now links data from 14 state and metropolitan HIV/AIDS registries across the United States with corresponding cancer registries. DCEG researchers have been able to show how AIDS-related cancer trends in the United States have changed since the HIV epidemic began, including the impact of the introduction of highly active antiretroviral therapy in 1996, through the mid-2000s. Over this time, individuals with HIV have experienced dramatic improvements in survival and are now reaching ages when cancer is commonly diagnosed. The population of U.S. residents living with HIV quadrupled between 1991 and 2005, and the average age of this group has risen substantially. Recent DCEG work is focusing on the long-term effects of



Eric Engels and Meredith Shiels.

chronic HIV infection and the ways in which cancer affects individuals with HIV as they age.

Meredith Shiels, Ph.D., a research fellow in IIB, recently described the new

PATRICIA HARTGE RECEIVES MAJOR HHS AWARD

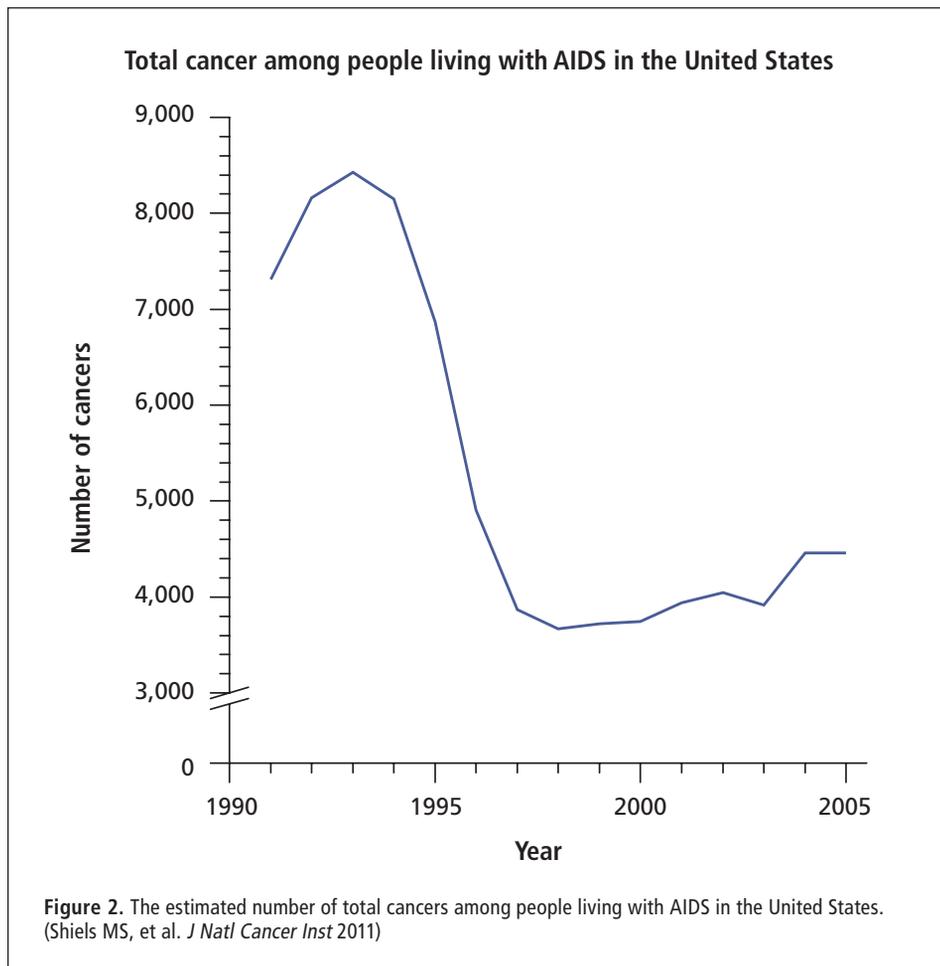


Patricia Hartge receives the Career Achievement Award from HHS Secretary Kathleen Sebelius.

In February, **Patricia Hartge, Sc.D.**, Deputy Director of DCEG’s Epidemiology and Biostatistics Program, received the Department of Health and Human Services (HHS) Career Achievement Award at the 2011 HHS Honor Awards Ceremony. In bestowing this award, HHS commended Dr. Hartge for her exceptional leadership in the fields of molecular, genetic, and clinical epidemiology.

Over her decades of service to NCI, Dr. Hartge’s innovative approach to the solution of complex epidemiologic questions has revolutionized the study of cancer in human populations. For example, she introduced the use of SEER (Surveillance, Epidemiology and End Results) registry data for rapid studies of cancer etiology; pioneered novel approaches for control selection; and instituted pooling protocols for large, multicenter studies of uncommon cancers. The studies that Dr. Hartge designed and conducted have made major contributions to our understanding of many malignancies, including cancers of the bladder, ovary, pancreas, and breast, as well as lymphoma.

—Jennifer Loukissas, M.P.P.



landscape of cancer risk and burden among the HIV-infected population in the United States (*Journal of the National Cancer Institute*, May 2011, see Figure 2). Based on an analysis of

data from the HACM Study, she showed that the number of AIDS-defining cancers (Kaposi sarcoma, NHL, and cervical cancer) has declined threefold (from 34,580 to 10,320 cases), while the

number of other non-AIDS-defining cancers has tripled (from 3,200 to 10,000 cases). “We know that some of the more common non-AIDS-defining cancers diagnosed in this population are due to viral co-infection, such as hepatitis B or C viruses or human papillomavirus, or are related to smoking, which is much more common among the HIV/AIDS population than the general U.S. population,” said Dr. Shiels. “The results underscore the magnitude of the cancer burden that will continue to rise as this population ages and the need for surveillance and screening grows.”

To define these trends further, Drs. Engels and Shiels are working with **Ruth M. Pfeiffer, Ph.D.**, Biostatistics Branch, and other scientists to take a closer look at how HIV has influenced overall cancer rates in the general population. They recently estimated that 28 percent of anal cancer cases in men and 1 percent of cases in women in the United States between 2001 and 2005 occurred among the HIV-infected population. Anal cancer is rare in the United States, but its rates have been rising steadily for several decades. The large size of the HACM Study allowed investigators to estimate general population incidence rates with and without HIV-infected cases and to show for the first time that the rates of anal cancer over time in men have been influenced substantially by HIV-infected cases.

Examining cancer trends in large registry-based resources has been critical for understanding cancer risk in immunosuppressed populations in the United States, Dr. Engels stated. “There’s still a lot we’re trying to learn about what’s driving the increased risk for certain cancers, and hopefully we can identify mechanisms so that the cancer risks in these populations can be minimized.” ■

QING LAN RECEIVES NIH OUTSTANDING MENTOR AWARD

In January, **Qing Lan, M.D., Ph.D., M.P.H.**, a senior investigator in the Occupational and Environmental Epidemiology Branch, received an Outstanding Mentor Award from the NIH Graduate Partnerships Program (GPP). Every year, GPP graduate students have the opportunity to nominate mentors for their leadership, dedication, and contributions to the students’ ability to conduct scientific research, communicate effectively, and network successfully. Dr. Lan was among three exceptional mentors across NIH chosen for recognition. The award was presented to Dr. Lan during the Eighth Annual NIH Graduate Student Research Symposium at the Natcher Conference Center.



Qing Lan

—Alyssa M. Voss, M.P.H.

MOLECULAR EPIDEMIOLOGY BOOK PUBLISHED

In April, *Molecular Epidemiology: Principles and Practices* was published as an International Agency for Research on Cancer (IARC) Scientific Publication.

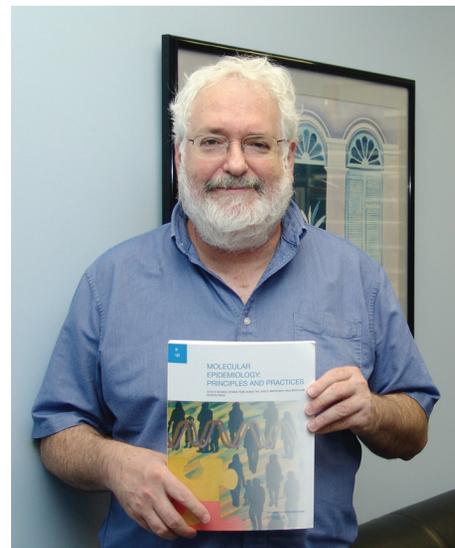
Nathaniel Rothman, M.D., M.P.H., M.H.S., a senior investigator and head of molecular epidemiology studies in the Occupational and Environmental Epidemiology Branch (OEEB), is the lead editor for the book. Other editors include Dr. Pierre Hainaut of IARC in Lyon, France; Dr. Paul Schulte of the National Institute for Occupational Safety and Health in Cincinnati, Ohio; Dr. Martyn Smith of the University of California, Berkeley; Dr. Paolo Boffetta of the Mount Sinai School of Medicine in New York, New York; and Dr. Frederica Perera of the Columbia University Mailman School of Public Health in New York, New York.

The text covers the major conceptual issues in molecular epidemiology with a strong emphasis on study design. Sixty-five authors contributed to the book, which has 27 chapters organized into 5 sections: (1) Contextual framework for molecular epidemiology, (2) Biomarkers—Practical aspects, (3) Assessing exposure to the environment, (4) Incorporating biomarkers into epidemiology study designs, and (5) Application of biomarkers to disease. The book is both a cornerstone for specialists and a teaching and training tool for public health, biology, and medical students. Dr. Rothman plans to use the text for the next DCEG molecular epidemiology course.

Joseph F. Fraumeni, Jr., M.D., Director of DCEG, wrote a foreword for the book, noting, “At this critical moment in the evolution of molecular epidemiology, the editors of this volume have enlisted

scientific leaders in the field to review the major concepts, methods, and tools of this interdisciplinary approach.... With the evidence in this volume as a starting point, the stage is set for basic, clinical, and population scientists to accelerate collaborative efforts that will contribute new biological insights and augment strategies for preventing and controlling disease on a global scale.”

Several DCEG staff contributed to the text, including **Christian C. Abnet, Ph.D., M.P.H.**, Nutritional Epidemiology Branch (NEB); **Neil E. Caporaso, M.D.**, Chief of the Genetic Epidemiology Branch; **Stephen J. Chanock, M.D.**, Chief of the Laboratory of Translational Genomics and Director of the Core Genotyping Facility (CGF); **Nilanjan Chatterjee, Ph.D.**, Chief of the Biostatistics Branch; **Amanda J. Cross, Ph.D.** (NEB); **Marianne K. Henderson,**

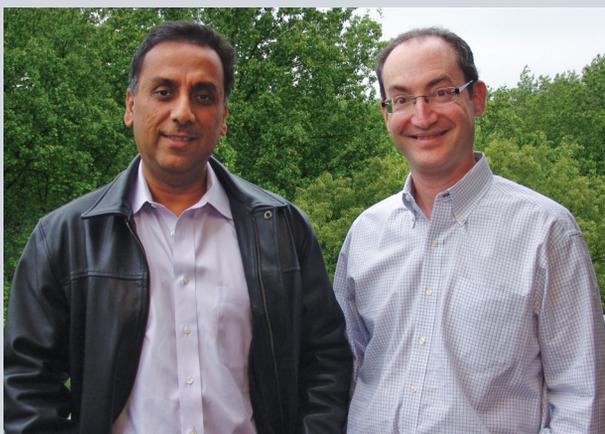


Nathaniel Rothman with a copy of *Molecular Epidemiology: Principles and Practices*.

M.S., Chief of the Office of Division Operations and Analysis; **Kevin B. Jacobs** (CGF); **Qing Lan, M.D., Ph.D., M.P.H.** (OEEB); and **Rashmi Sinha, Ph.D.** (NEB). ■

CHATTERJEE AND ENGELS ELECTED TO AMERICAN EPIDEMIOLOGICAL SOCIETY

In March, **Nilanjan Chatterjee, Ph.D.**, Chief of the Biostatistics Branch, and **Eric A. Engels, M.D., M.P.H.**, a senior investigator in the Infections and Immunoepidemiology Branch, were elected to the American Epidemiological Society (AES) at the Society's annual meeting in Berkeley, California. The mission of the AES is to provide a scientific forum for senior epidemiologists, who engage in a



Nilanjan Chatterjee and Eric Engels.

lively interchange of ideas with their peers at the annual meetings. Nominees are evaluated on the basis of the quality and impact of their epidemiologic accomplishments and contributions; academic activities, such as teaching and mentoring; and other aspects of professional work, including administrative leadership and community service.

NICOLAS WENTZENSEN EXPLORES MARKERS FOR GYNECOLOGIC CANCERS

Scientists are developing a better understanding of the relationship between human papillomavirus (HPV) and cervical cancer due to the efforts of researchers like **Nicolas Wentzensen, M.D., Ph.D.**, a tenure-track investigator in the Hormonal and Reproductive Epidemiology Branch (HREB). In 2007, Dr. Wentzensen joined NCI as a visiting fellow from Heidelberg University in Germany, where he earned his M.D. and a Ph.D. in applied tumor biology. Dr. Wentzensen has always been interested in the etiology of cancers, and his clinical background helped guide his interest toward population-based research. He currently studies the origins of several gynecologic cancers and how to use that knowledge to improve screening and prevention efforts.

Dr. Wentzensen has been interested in cervical cancer for more than 15 years. Although it is known that infection with

HPV causes cervical cancer, many HPV-infected women never develop cancer. In addition, women can be infected with multiple HPV strains of which only some may increase cancer risk. Research into what factors drive cancer formation, and the discovery of biomarkers that are harbingers of cancer progression, will allow more informed screening strategies to identify women most at risk of cervical cancer and to reduce unwarranted testing in women at low risk.

Dr. Wentzensen and his colleagues, including **Mark Schiffman, M.D., M.P.H.**, a senior investigator in the Clinical Genetics Branch, recently found that although women may be infected with multiple HPV types, only one HPV strain, HPV 16, predominated in the discrete cervical biopsies in which precancerous cells were apparent. “This discovery confirms the dominant role of the HPV 16 strain in the causation



Nicolas Wentzensen

of cervical cancer,” Dr. Wentzensen explained, “and contributes to data that indicate that screening women for specific HPV strains could identify those women most at risk of developing cancer.”

The American Cancer Society Screening Guidelines for the Prevention and Early Detection of Cervical Cancer, released this year, recommend HPV DNA and cytology (Pap smear) co-testing as a primary screening measure in women aged 30 to 65 years. Dr. Wentzensen was a member of one of the working groups for these guidelines. “These guidelines reflect the current evidence for HPV testing in cervical cancer,” Dr. Wentzensen said. “In addition to identifying women at risk of developing cervical cancer, it is clear that HPV-negative women do not require rigorous follow-up, allowing them to avoid unnecessary testing.” He believes that in the future, HPV detection and biomarker analysis could potentially take the place of all routine Pap smears. “Although we still need more evidence, it is likely that these HPV-based tests will allow more accurate prediction of a woman’s risk of developing cervical cancer than cytological tests,” he noted.

WILLIAM ANDERSON RECEIVES SCIENTIFIC TENURE

In March, NIH awarded scientific tenure to **William F. Anderson, M.D., M.P.H.**, Biostatistics Branch (BB). Dr. Anderson, who received his training at Tulane University School of Medicine in New Orleans, Louisiana, is board certified in internal medicine, hematology, and medical oncology. He served as a private practitioner in medical oncology/hematology for 16 years in rural northeast Louisiana before coming to NCI as a Cancer Prevention Fellow and later a medical officer with the Division of Cancer Prevention. In 2005, Dr. Anderson joined BB as a tenure-track investigator to develop and lead a highly collaborative research program in descriptive epidemiology using biostatistical models and methods to generate new clues to cancer etiology based on the morphologic and molecular heterogeneity of breast and other cancers.

Dr. Anderson is the senior editor for the Cancer Surveillance Research section of the journal *Cancer Epidemiology, Biomarkers & Prevention*, and he serves on the editorial boards for *Breast Cancer Research and Treatment* and the *Journal of Clinical Oncology*. In addition, he is an adjunct professor of pathology at the George Washington University School of Medicine and Health Sciences in Washington, D.C., and an adjunct professor of preventive medicine and biometrics at the Uniformed Services University of the Health Sciences in Bethesda, Maryland.



William Anderson

Dr. Wentzensen has investigated several viral and cellular characteristics that differ between normal and precancerous cervical cells in efforts to discover biomarkers of cancer progression. One characteristic under study is the methylation of HPV and host cell DNA, a phenomenon that Dr. Wentzensen examined in a large, population-based study at Kaiser Permanente in Northern California. In women infected with the most carcinogenic types of HPV, researchers found that methylation at specific sites in the HPV genome was more common in precancerous cells than in normal cells infected with HPV. Dr. Wentzensen has received several NCI competitive funding awards for his work on DNA methylation in gynecological cancers, including an NCI Director's Intramural Innovation Award in 2012 to enable him to develop an HPV methylation assay.

Another potential biomarker for cervical cancer is the overexpression of p16, a cellular factor that Dr. Wentzensen

translated to clinical application in his work at Heidelberg University. He now works with collaborators to assess the predictive potential of p16 in cytological samples from the Costa Rica HPV Vaccine Trial. Dr. Wentzensen also is collaborating with Kaiser Permanente to assess p16 as part of primary screening for cervical cancer. In addition, he complements his biomarker efforts by working with **Sholom Wacholder, Ph.D.**, a senior investigator in the Biostatistics Branch, on principles of using biomarkers for risk stratification.

In contrast to cervical cancer, scientists have a more limited understanding of the origins of ovarian cancer, in part because ovarian cancer is highly heterogeneous, appearing in multiple forms. **Louise A. Brinton, Ph.D.**, Chief of HREB, and Dr. Wentzensen are investigating a number of ovarian cancer risk factors, including oral contraceptive use and body mass index, which differ by cancer subtype. Dr. Wentzensen, together with **Patricia Hartge, Sc.D.**, Deputy Director

of the Epidemiology and Biostatistics Program, and extramural collaborators, is striving to create an ovarian cancer cohort consortium. "One goal of this work," Dr. Wentzensen said, "is to improve the risk prediction models for ovarian cancer." Similar to his work in cervical cancer, Dr. Wentzensen, with **Mark E. Sherman, M.D.**, a senior clinician in HREB, is studying DNA methylation in ovarian cancer to determine whether differential methylation patterns correlate with distinct cancer subtypes.

Dr. Wentzensen joined NCI because it is home to leaders in HPV and cervical cancer. He enjoys the breadth of expertise among his colleagues. "It is difficult to name just a few key collaborators here at NCI, because the list is so long," he said. "And it isn't just principal investigators and staff scientists; students and fellows have made important contributions to this research. These projects are team efforts, and mentoring plays an integral role in this work." ■

—Amber K. Boehm, Ph.D.

DCEG RESEARCH INFORMS NEW CERVICAL CANCER SCREENING GUIDELINES

The U.S. Preventive Services Task Force (USPSTF), an independent panel of experts in prevention and evidence-based medicine from outside the federal government, recently published new guidelines for cervical cancer screening. Three health organizations—the American Cancer Society, the American Society for Clinical Pathology, and the American Society for Colposcopy and Cervical Pathology—also have released new cervical cancer screening guidelines.

Although the USPSTF and the three health organizations developed their guidelines independently, their recommendations are consistent with one another. The USPSTF recommends screening with cytology (Pap test) for women aged 21 to 65 every three years. Women aged 30 to 65 can safely

extend the screening interval to once every five years if they undergo concurrent human papillomavirus (HPV) testing with the Pap test. Screening is not recommended for women younger than 21 years, women older than 65 years who have had adequate prior screening and are not otherwise at high risk of cervical cancer, or women who have had a hysterectomy with removal of the cervix and do not have a history of high-grade precancerous lesions (i.e., grade 2 or 3 cervical intraepithelial neoplasia) or cervical cancer. Furthermore, the USPSTF recommends against screening for cervical cancer with HPV testing, alone or in combination with cytology, in women younger than 30 years.

Revisions of the guidelines were informed by results from POBASCAM (Population-Based

Screening Study Amsterdam), a randomized controlled trial for implementation of high-risk HPV testing in cervical cancer screening, and a population-based study in routine clinical practice conducted by **Hormuzd A. Katki, Ph.D.**, Biostatistics Branch, and colleagues, which included nearly 332,000 women who underwent both HPV and Pap testing at Kaiser Permanente Northern California. Details of Dr. Katki's study, titled "Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: A population-based study in routine clinical practice," were published in *Lancet Oncology*, and a summary of the results is available in the March 2012 issue of *Linkage*.

—Wendy Schneider-Levinson

DCEG HOSTS VISITING SCHOLAR GRAHAM COLDITZ

In December, DCEG welcomed Visiting Scholar Dr. Graham A. Colditz. Dr. Colditz is Associate Director for Prevention and Control at the Alvin J. Siteman Cancer Center, Washington University School of Medicine and Barnes-Jewish Hospital, in St. Louis, Missouri. He also is the Niess-Gain Professor of Surgery and Professor of Medicine as well as the Chief of the Division of Public Health Sciences within the Department of Surgery at the Washington University School of Medicine. Dr. Colditz is renowned for his research related to the etiology and prevention of chronic disease and for his work with the Harvard Nurses' Health Study.

Dr. Colditz received an M.B.B.S. from the University of Queensland in Brisbane, Australia, and an M.P.H. and Dr.P.H. in epidemiology from the Harvard School of Public Health in Boston, Massachusetts. He later received his M.D. from the University of Queensland.



Gretchen Gierach, Robert Hoover, Graham Colditz, and Patricia Hartge.

Dr. Colditz has a longstanding interest in the causes and prevention of breast and other malignancies among women. From 1999 to 2006, he served as principal investigator of the Nurses' Health Study, a landmark cohort study that follows U.S. women with questionnaire assessment of lifestyle factors and

the use of biomarkers to assess risk of chronic diseases. Dr. Colditz's expertise includes the formulation of cancer risk prediction models, including the "Your Disease Risk" model, which provides personalized risk estimates for cancer, heart disease, stroke, diabetes, and osteoporosis. Dr. Colditz has worked with state and national organizations, including NIH, to translate research findings into public health strategies for disease prevention.

Dr. Colditz has received numerous awards and honors throughout his career. In 2011, he received the American Cancer Society's Medal of Honor for Cancer Control Research, which acknowledged his significant contributions toward understanding the causes and prevention of cancer. He also has been awarded the DeWitt S. Goodman Memorial Lectureship by the American Association for Cancer Research. He is a Fellow of the Australian Faculty of Public Health Medicine, a faculty of the Royal Australian College of Physicians.

SPECIAL STUDIES IRB IMPLEMENTS NEW WEB-BASED SYSTEM

In December, the NCI Special Studies Institutional Review Board (SSIRB) implemented the Integrated Research Information System (iRIS), a web-based application designed to help create, manage, and process research protocols. The advantages of iRIS include increased efficiency in processing and tracking submissions; centralized, consistently maintained, and easily accessible records; and a substantial reduction in paper waste. DCEG's move to iRIS also creates consistency across NCI because the NCI Center for Cancer Research (CCR) and the NCI Deputy Ethics Counselor have used iRIS for several years. Several DCEG staff helped with the implementation of iRIS, including **Renée Bremer, M.S.**, Clinical Genetics Branch; **David P. Check**, Biostatistics Branch (BB); **Marianne K. Henderson, M.S.**, Chief of the Office of Division Operations and Analysis (ODOA); **Carl McCabe, Ph.D.** (ODOA); **Susan Privot**, Office of Communications and Special Initiatives; **Catherine Schairer, Ph.D.**, staff scientist in BB and chair of the SSIRB; and **Shelia Hoar Zahm, Sc.D.**, scientific advisor (contractor) in DCEG's Office of the Director. Marianne Nogle, administrator in the Protocol Review Office of CCR, also helped DCEG implement iRIS.

More information about iRIS and the SSIRB can be found on the DCEG intranet or from the SSIRB coordinators (ncissirbcoordinators@mail.nih.gov).

—David P. Check

In addition, he is an elected member of the Institute of Medicine of the National Academies.

Patricia Hartge, Sc.D., Deputy Director of DCEG's Epidemiology and Biostatistics Program, welcomed Dr. Colditz, who began his two-day visit with a seminar titled "Breast and colon cancer: Risk accumulation and prevention." Dr. Colditz stated that more than half of cancer incidence and mortality could be prevented by applying current knowledge. His comments focused on his research on lifestyle factors, such as alcohol, which has been shown to be associated with breast cancer. He emphasized the role in risk accumulation

**"To maximize benefits,
we must focus on biologically
relevant time periods."**

played by the timing of exposures during a person's life, noting that hormonal status and other exposures during adolescence may be particularly important. He remarked that "to maximize benefits, we must focus on biologically relevant time periods." Dr. Colditz concluded with recommendations for ways to move forward with cancer prevention, including encouraging research to elucidate how best to communicate results effectively to the public and to encourage people to engage in health-promoting behaviors.

During his visit, Dr. Colditz participated in several meetings with DCEG scientists. **Gretchen L. Gierach, Ph.D.**, Hormonal and Reproductive Epidemiology Branch (HREB), moderated a session on "Recent leads in breast cancer epidemiology"; **Ruth M. Pfeiffer, Ph.D.**, Biostatistics Branch, led a session on "Topics and recent developments

in cancer risk prediction"; and **Mark Purdue, Ph.D.**, Occupational and Environmental Epidemiology Branch, led a discussion on "Rapid follow-up of molecular epidemiology observations." Dr. Colditz also met with DCEG fellows during a brown-bag lunch. The discussion, facilitated by **Gwen Murphy, Ph.D., M.P.H.**, Nutritional Epidemiology Branch, and **Cher Dallal, Ph.D.** (HREB), touched on the role of

epidemiologists in translating research into cancer prevention strategies.

Reflecting on his time as a Visiting Scholar, Dr. Colditz said, "I enjoyed the stimulating discussions during my visit to DCEG. I developed new ideas for potential collaborations and hope others did too." ■

—Saloni Nayar, M.P.H.

DCEG FELLOWS PRESENT AT THE 2012 NIH SPRING RESEARCH FESTIVAL

In April, six DCEG postbaccalaureate fellows and one Howard Hughes Medical Institute (HHMI)–NIH Research Scholar presented posters as part of the 2012 NIH Spring Research Festival, a two-day event sponsored by the NIH Office of Intramural Training and Education. The NIH-wide festival included poster presentations by nearly 300 postbaccalaureate fellows as well as fellows in the Clinical Research Training Program and the HHMI–NIH Research Scholar Program. **Laura Linville**, of the Hormonal and Reproductive Epidemiology Branch (HREB), received special recognition for a poster that scored among the top 20 percent of those presented.

The following DCEG posters were displayed at the festival:

The relation of PLCE1 protein expression to genotype and survival in esophageal squamous cell carcinoma

Victoria Burton, Genetic Epidemiology Branch (GEB)

Mentors: **Philip R. Taylor, M.D., Sc.D.** (GEB), and **Stephen M. Hewitt, M.D., Ph.D.**, Laboratory of Pathology, NCI Center for Cancer Research

Following up on GWAS peaks in chromosome 1 to identify novel mutations in SETDB1 and other candidate genes leading to increased melanoma susceptibility

Wendy Kim, Laboratory of Translational Genomics (LTG)

Mentor: **Kevin Brown, Ph.D.** (LTG)

Systemic inflammatory cytokine levels and relationship with human papillomavirus infection in rural Nigerian women

Christine Kiruthu, Infections and Immunoepidemiology Branch (IIB)

Mentor: **Sam M. Mbulaiteye, M.D.** (IIB)

Variation in zinc finger region of PRDM9 changes the landscape of hotspot recombination

Joseph Kovacs (LTG)

Mentor: **Stephen J. Chanock, M.D.**, Chief of LTG and Director of the Core Genotyping Facility

Associations between breast cancer risk factors and terminal ductal lobular unit (TDLU) involution in normal breast and benign breast disease tissues

Laura Linville (HREB)

Mentors: **Gretchen L. Gierach, Ph.D.**, and **Jonine D. Figueroa, Ph.D., M.P.H.** (both of HREB)

Functional characterization of pancreatic cancer susceptibility variants on Chr1q32

Abbey Thompson (LTG)

Mentor: **Laufey Amundadottir, Ph.D.** (LTG)

Patterns of common adult bone sarcomas as a second malignancy in relation to radiotherapy

Lindsey Wu, HHMI–NIH Research Scholar, Radiation Epidemiology Branch (REB)

Mentor: **Amy Berrington de González, D.Phil.** (REB)

DCEG HOSTS VISITING SCHOLAR DAVID SCHOTTENFELD

In May, DCEG welcomed Dr. David Schottenfeld as a Visiting Scholar. Dr. Schottenfeld is the John G. Searle Professor Emeritus of Epidemiology at the University of Michigan School of Public Health and Professor Emeritus of Internal Medicine at the University of Michigan Medical School in Ann Arbor. He is a renowned researcher whose contributions to the field of cancer epidemiology span the past 50 years. In addition, he is a prolific writer and co-edited the definitive textbook *Cancer Epidemiology and Prevention* with **Joseph F. Fraumeni, Jr., M.D.**, Division Director.

Dr. Schottenfeld received his M.D. from Cornell University Medical College in New York, New York, and completed training in internal medicine, medical oncology, epidemiology, and preventive medicine. From 1963 to 1986, he directed research and training programs in cancer epidemiology and prevention at Memorial Sloan-Kettering Cancer Center and Cornell University Medical College, both in New York. In 1986, Dr. Schottenfeld was appointed chair of the Department of Epidemiology and John G. Searle Professor of Epidemiology at the University of Michigan School of Public Health.

Dr. Schottenfeld has received numerous honors throughout his career, including an Academic Career Award in Preventive Oncology from NCI, the Abraham Lilienfeld Award from the American College of Epidemiology, the John Snow Award from the American Public Health Association, the Harvard School of Public Health Alumni Award of Merit, and the James D. Bruce Memorial Award for distinguished contributions in preventive medicine from the American College of Physicians. Dr. Schottenfeld is a founding member and former president



Joseph Fraumeni, David Schottenfeld, and Robert Hoover.

of the American Society of Preventive Oncology and past president of the Society for Epidemiologic Research.

Robert N. Hoover, M.D., Sc.D., Director of the Epidemiology and Biostatistics Program, welcomed Dr. Schottenfeld and applauded his achievements as a true generalist in the field of cancer epidemiology with seminal findings across a wide range of cancers and exposures. Dr. Schottenfeld began his two-day visit with a seminar titled “Quantitative assessment of avoidable causes of cancer in the United States: What have we learned since the 1981 Doll-Peto publication?” He gave an overview of the seminal report by Dr. Richard Doll and Dr. Richard Peto, which quantified the contributions of various environmental and lifestyle factors to cancer incidence and mortality. “It is a remarkable and thoughtful document that has been challenging us for years,” Dr. Schottenfeld said.

In their paper, Drs. Doll and Peto concluded that theoretically, 75 to

80 percent of cancer deaths in the United States could have been avoided. In an effort to reassess and update their findings, Dr. Schottenfeld conducted a comprehensive review of epidemiologic studies published since 1981. He analyzed relative risks of cancer for eight environmental and lifestyle exposures and compared estimated population attributable fractions (used to quantify the proportion of cases that would not have occurred in the absence of exposure) in the United States, the United Kingdom, and France to those estimated by Drs. Doll and Peto. Dr. Schottenfeld then offered a current assessment of selected avoidable causes of cancer, including tobacco, alcohol, infectious agents, and obesity and physical inactivity.

Based on his research, Dr. Schottenfeld believes that as much as 50 to 60 percent of cancer deaths in the United States could be avoided today. “I hope that this effort will stimulate the public health community to recognize the need for more precise estimates if we’re going to

advance our efforts of controlling cancer,” Dr. Schottenfeld said.

Later in his visit, Dr. Schottenfeld participated in a panel discussion with Dr. Fraumeni on “Cancer epidemiology over the last half-century and thoughts on the future.” Dr. Hoover moderated the event, which he described as “a unique opportunity to hear an oral history of the discipline of cancer epidemiology from two legends in the field.”

Drs. Fraumeni and Schottenfeld spoke candidly about their past mentors and colleagues, noteworthy contributions to the field, and how cancer epidemiology has evolved as a discipline during their lifetimes. They ended the discussion with a look toward the future. “Though

we have made great strides during the past few decades, there are still so many opportunities in the field and so much that remains to be learned,” Dr. Fraumeni said.

During his visit, Dr. Schottenfeld also attended individual and group meetings with DCEG scientists. The Immune Markers Working Group hosted a roundtable discussion on DCEG efforts to evaluate immunologic and inflammation biomarkers of cancer risk. Several Division staff members gave updates on their research projects, including **Clara Bodelon, Ph.D., M.S.**, Hormonal and Reproductive Epidemiology Branch; **Anil K. Chaturvedi, Ph.D.**, Infections and Immunoepidemiology Branch (IIB); **Allan Hildesheim,**

Ph.D., Chief of IIB; **Wen-Yi Huang, Ph.D., M.S.P.H.**, Occupational and Environmental Epidemiology Branch (OEEB); and **Mark Purdue, Ph.D.** (OEEB). Dr. Schottenfeld also met with DCEG fellows during an informal brown-bag lunch, where he spoke about the highlights of his career, including his experience as a director of training programs and as co-editor of the book *Cancer Epidemiology and Prevention*.

“Though I have been to DCEG many times before, this visit seems very special,” Dr. Schottenfeld said. “I have so many colleagues and friends in the Division, and I always look forward to my return.” ■

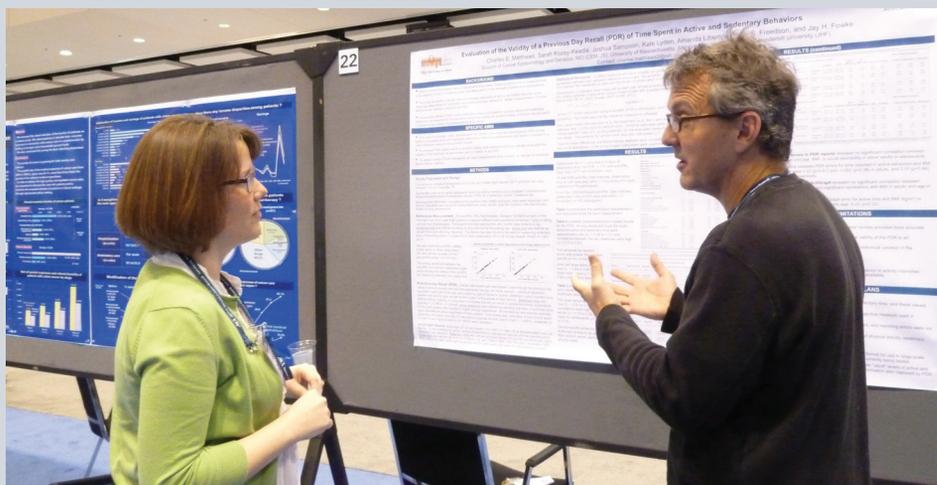
—Victoria A. Fisher, M.P.H.

DCEG PARTICIPATES IN THE ANNUAL AACR MEETING

In April, several DCEG staff members participated in the annual meeting of the American Association for Cancer Research (AACR) in Chicago, Illinois. This five-day event highlighted the latest scientific advances in basic, clinical, and epidemiologic cancer research. The theme of this year’s meeting was Accelerating Science: Concept to Clinic.

Stephen J. Chanock, M.D., Chief of the Laboratory of Translational Genomics and Director of the Core Genotyping Facility, and **Allan Hildesheim, Ph.D.**, Chief of the Infections and Immunoepidemiology Branch (IIB), gave presentations at major symposia during the meeting. Dr. Chanock spoke on “Genome-wide association studies in cancer: A step in the right direction,” and Dr. Hildesheim discussed “Epstein-Barr virus and cancer: Opportunities for etiologic research and prevention.”

During the symposium “Cancer risk, immunity, and inflammation,” **Todd M. Gibson, Ph.D.**, Radiation Epidemiology Branch (REB), presented “Risk of diffuse large B-cell lymphoma in solid organ transplant recipient.” Dr. Gibson received an AACR Scholar-in-Training Award for this paper from the AACR Molecular Epidemiology Working Group.



Britton Trabert and Charles Matthews discuss a poster at the annual AACR meeting.

In addition, **Vladimir Drozdovitch, Ph.D.** (REB), spoke on “Thyroid doses in the exposed populations: How Fukushima compares to Chernobyl and other nuclear reactor accidents”; **Maureen C. Hatch, Ph.D.** (REB), presented “Epidemiology of thyroid cancer after the Chernobyl accident”; **Maria Teresa Landi, M.D., Ph.D.**, Genetic Epidemiology Branch, discussed “Inherited variation at chromosome 12p13.33 including *RAD52* influences the risk of squamous cell lung

cancer risk”; and **Meredith Shiels, Ph.D.** (IIB), gave an “Update on HIV and cancer.” **Jackie Lavigne, Ph.D., M.P.H.**, Chief of DCEG’s Office of Education, served as a roundtable mentor during a professional advancement session on “The career development plan: Taking charge of your career,” organized by the AACR Associate Member Council. DCEG scientists also presented more than 30 posters at the meeting.

PETER KRAFT PRESENTS 2012 ROBERT A. WELCH MEMORIAL LECTURE

In January, the Laboratory of Translational Genomics hosted Dr. Peter Kraft, an associate professor in the Departments of Epidemiology and Biostatistics at the Harvard School of Public Health in Boston, Massachusetts, as an invited speaker for the Robert A. Welch Memorial Lecture.

Dr. Kraft's work focuses on statistical approaches for integrating gene-environment interactions into genome-wide association studies (GWAS), methods for pathway analysis incorporating genetic variants from functionally related genes, and risk prediction models when multiple variants are identified from GWAS. Dr. Kraft collaborates in consortial GWAS of breast, prostate, and pancreatic cancers. In addition, he actively contributes to the statistical working group within the international Breast and Prostate Cancer Cohort Consortium.



Peter Kraft and Stephen Chanock.

During his visit, Dr. Kraft presented a seminar titled "Leveraging gene-gene and gene-environment interactions to understand cancer risk." He discussed different statistical approaches for investigating gene-environment interactions in the context of GWAS,

including standard logistic regression, semi-parametric maximum-likelihood estimation of an empirical Bayes shrinkage estimator, and a joint test for genetic main effects and interactions. Dr. Kraft explained how these interactions can be used to identify new variants that may have been missed in GWAS and how to leverage assumed effect modifiers and increase statistical power. He also discussed the impact of these interactions on risk prediction and prognostic models.

The Robert A. Welch Memorial Lecture was established in honor of the late Robert A. Welch, M.S., founding Director of Operations at the NCI Core Genotyping Facility (CGF). Mr. Welch played a key role in developing and managing CGF and its large-scale studies of the cancer risks associated with common genetic variations. His commitment and leadership inspired his colleagues both at CGF and elsewhere and were central to the success of CGF, which continues to work toward his vision. ■

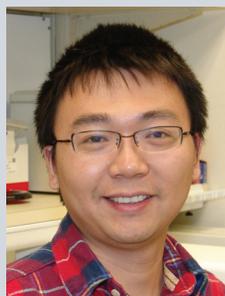
—Marie-Joséphine Horner, M.S.P.H.

THIRD ROBERT A. WELCH FELLOWSHIP AWARDED TO WEI TANG

Wei Tang, Ph.D., of the Laboratory of Translational Genomics (LTG), has been chosen to receive the third Robert A. Welch Fellowship. Dr. Tang joined LTG as a postdoctoral fellow in 2009. Under the guidance of Ludmila Prokunina-Olsson, Ph.D. (LTG), Dr. Tang is focusing his research on the fine-mapping of susceptibility loci from genome-wide association studies. One of his ongoing projects is to fine-map the regions containing *JAZF1* and *UGTA1*, which harbor prostate and bladder cancer susceptibility loci, respectively. In addition, Dr. Tang applies next-generation sequencing methods to analyze DNA, RNA-seq (transcriptome sequencing), and ChIP-seq (chromatin immunoprecipitation sequencing) to detect single nucleotide polymorphisms, splicing forms, and novel transcripts that might be associated with cancer.

Dr. Tang earned his Ph.D. at the Bio-X Center of Shanghai Jiao Tong University in China. Under the mentorship of Center Director Dr. Lin He, Dr. Tang focused his research on the genetics of schizophrenia, bipolar disorder, and other complex diseases.

The Robert A. Welch Fellowship is a competitive postdoctoral award within DCEG that supports mentored research in molecular epidemiology with special emphasis on the application of emerging genomic technology. The fellowship was established in honor of the late Robert A. Welch, M.S., founding Director of Operations at the NCI Core Genotyping Facility.



Wei Tang

BENCH-TO-BEDSIDE AWARD: POSTPARTUM EVENTS AND BREAST CANCER

Mark E. Sherman, M.D., senior clinician in the Hormonal and Reproductive Epidemiology Branch (HREB), and Dr. Kathleen Arcaro, associate professor in the Department of Veterinary & Animal Sciences at the University of Massachusetts, Amherst, have received an NIH Bench-to-Bedside Award for a project titled “Molecular epidemiology of postpartum involution of the breast: Development and demonstration of tools for understanding the postpartum period in relation to risk for early-onset breast cancer.” Drs. Sherman and Arcaro are leading a research team that includes Jane Balkam, Ph.D., a lactation consultant with the Nursing Mothers Program at the NIH Office of Research Services; David A. Bluemke, M.D., Ph.D., Director of Radiology and Imaging Sciences at the NIH Clinical Center; Jessica M. Faupel-Badger, Ph.D., M.P.H., Deputy Director of the NCI Cancer Prevention Fellowship Program; Kathleen C. Flanders, Ph.D., Laboratory of Cancer Biology and Genetics, NCI Center for Cancer Research (CCR); **Gretchen**

L. Gierach, Ph.D. (HREB); Stephen M. Hewitt, M.D., Ph.D., Laboratory of Pathology, CCR; and Dr. Alan Meeker, assistant professor of pathology and urology at the Johns Hopkins University School of Medicine in Baltimore, Maryland.

Studies of postpartum involution in animal models have suggested that processes that return the milk-producing breast to its native resting state (“post-weaning involution”) may affect the development of aggressive breast cancer. The “bench” aims of this project are to develop optimal methods for collecting and fractionating milk into liquid and cellular components that investigators can apply in large molecular epidemiological studies. The “bedside” aims of this project focus on evaluating these methods among first-time African American and white mothers of varying ages. The long-term goal is to develop the optimal means for milk collection and processing for large epidemiological studies of the risk of early-onset, aggressive breast cancers.

Dr. Arcaro will collaborate with Dr. Sherman and other DCEG investigators to extend her research on detecting DNA methylation silencing of tumor suppressor genes using DNA isolated from cells shed in milk. In collaboration with Dr. Bluemke, the researchers will explore the use of postpartum magnetic resonance imaging to understand the origins of topographic variation in the breast. If successful, this project will identify methods that future studies can use to combine analyses of milk and radiological imaging for assessing the risk of early-onset breast cancers, which disproportionately affect African Americans.

The NIH Bench-to-Bedside Award Program fosters collaboration among laboratory, clinical, and population scientists in efforts to improve understanding of important disease processes that may lead to new therapeutic, preventive, or diagnostic interventions. ■

—Mark E. Sherman, M.D.

WORKSHOP ON POSTPARTUM BREAST REMODELING, LACTATION, AND CANCER RISK

Childbearing, lactation, and physiological processes that remodel the breast after weaning are strongly implicated in the development of breast cancer, but the biology of these events is poorly understood. To identify important research questions on these topics and facilitate multidisciplinary collaboration among scientists and health professionals, DCEG’s Hormonal and Reproductive Epidemiology Branch (HREB) and the NIH Office of Research on Women’s Health convened a workshop in March. **Mark E. Sherman, M.D.**, senior clinician in HREB, and Jessica M. Faupel-Badger, Ph.D., M.P.H., Deputy Director of the NCI Cancer Prevention Fellowship Program, cochaired the workshop. The program included discussions on the epidemiology of

breastfeeding and breast cancer risk, mouse models of pregnancy and postpartum mammary gland remodeling, and the use of breast milk as a biological specimen for research.

Increasing the frequency and duration of breastfeeding in the United States is one of the goals of the Healthy People 2020 initiative because lactation has numerous established health benefits for both mothers and infants. Lactation is associated with reduced breast cancer risk, and emerging results suggest that the protection is greatest for basal breast cancers, which disproportionately affect African American women. These types of breast cancers often occur before women start undergoing routine mammographic

screening, are difficult to detect by screening, and are challenging to treat.

The workshop highlighted advances in the use of breast milk to study biomarkers (including inflammatory markers and glycoproteins) and mechanisms (such as silencing of tumor suppressor genes via DNA methylation) that could be useful for risk assessment, early detection, or prevention of breast cancer. Participants expressed strong enthusiasm for continued interactions to advance this field and for meeting again in conjunction with national meetings.

—Mark E. Sherman, M.D., and
Jessica M. Faupel-Badger, Ph.D., M.P.H.

FOURTH ANNUAL DCEG FELLOWS' TRAINING SYMPOSIUM

In March, DCEG held the fourth Annual Fellows' Training Symposium, titled Exploring Uncharted Territories in Cancer Research. The event was sponsored by DCEG's Office of Education (OE) and organized by a DCEG fellows committee, including cochairs **Hannah Arem, M.H.S.**, Nutritional Epidemiology Branch (NEB), and **Patricia Luhn, Ph.D., M.P.H.**, Hormonal and Reproductive Epidemiology Branch (HREB), along with **Maria Constanza Camargo, Ph.D.**, Infections and Immunoepidemiology Branch (IIB), **Felipe Castro, Ph.D.** (IIB), **Benjamin Emmanuel, M.P.H.** (IIB), **Ashley S. Felix, Ph.D., M.P.H.** (HREB), **Roberto Flores, Ph.D., M.P.H.** (IIB), **Asieh Golozar, M.D., M.P.H.**, Genetic Epidemiology Branch, and **Farzana Walcott, M.D.**, Clinical Genetics Branch, with support from **Jackie Lavigne, Ph.D., M.P.H.**, Chief of OE, **Kristin Kiser, M.H.A., M.S.** (OE), and **Pamela Lotinsky** (OE). The aim of the



The Fellows' Training Symposium organizing committee and speakers: (front) Ashley Felix, Jackie Lavigne, Maria Constanza Camargo, Asieh Golozar, and Andrew Freedman; (middle) Robert Hoover, Kristen Kiser, Hannah Arem, Patricia Luhn, and Roberto Flores; (back) Felipe Castro and Faith Davis. (Not shown: Benjamin Emmanuel, Muin Khoury, Pamela Lotinsky, and Farzana Walcott.)

symposium was to explore opportunities both within and outside of DCEG for developing and performing innovative research. More than 75 predoctoral and postdoctoral fellows, representing all branches and laboratories of DCEG, participated in the event.

Dr. Faith Davis, chair of the Department of Public Health Sciences at the University of Alberta School of Public Health in Edmonton, Canada, began the symposium with a lecture titled "Uncharted territories: Reflections." Dr. Davis shared examples of unexpected opportunities and health inequities research that she pursued while focusing on her work in radiation epidemiology. She also offered advice to fellows about how to identify and pursue novel research questions specific to their interests.

Muin Khoury, M.D., Ph.D., Acting Associate Director of the Epidemiology and Genomics Research Program in NCI's Division of Cancer Control and Population Sciences (DCCPS) and Director of the Office of Public Health Genomics at the Centers for Disease Control and Prevention in Atlanta, Georgia, spoke on the topic "Public health genomics: From the science of discovery to the science of action." He emphasized the importance of finding a balance in the translation of genomics research so that useful interventions are

DCEG INVESTIGATORS PRESENT AT GLOBAL HEALTH MEETING

In March, NCI's Center for Global Health (CGH) held a meeting on "Setting Priorities for Global Cancer Research" to review NCI's current global health research portfolio. The meeting provided an opportunity to identify unmet research needs and areas of research in which NCI should strengthen its collaborations with U.S. and international agencies and organizations.

NCI Director Harold E. Varmus, M.D., and Ted Trimble, M.D., M.P.H., Director of CGH, offered opening remarks and goals for the meeting. Three DCEG investigators gave presentations during a session titled "Prevention, screening, and early diagnosis for certain cancers." **Allan Hildesheim, Ph.D.**, Chief of the Infections and Immunoepidemiology Branch (IIB), spoke about cervical cancer, which represents 10 percent of female cancers worldwide, with 80 percent of cases occurring in the developing world. **Ann W. Hsing, Ph.D.**, formerly of IIB, spoke on gallbladder cancer, which has large geographic variation with the highest rates reported in Chile, China, and India. **Philip R. Taylor, M.D., Sc.D.**, Genetic Epidemiology Branch, discussed squamous cell esophageal cancer; 83 percent of deaths from this cancer occur in the developing world. The highest rates are seen in eastern and central Asia, the east coast of Africa, and Uruguay.

Discussions and conclusions from the meeting will inform the drafting of recommendations for future research at CGH.

developed and delivered to the public. In addition, he shared his idea of knowledge integration, through which resources like the Human Genome Epidemiology Network (HuGENet) and the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative could be used for translating and evaluating genomic applications.

Andrew Freedman, Ph.D., Chief of the Clinical and Translational Epidemiology Branch in DCCPS, presented “New opportunities in molecular cancer epidemiology.” Dr. Freedman spoke about opportunities for integrating basic and clinical science for pharmaco-epidemiologic research and “getting the right medicine to the right person at the right time.”

Fellows had an opportunity to interact with the invited speakers at a panel discussion, during which the speakers answered scientific questions and offered advice.

The symposium included two poster sessions that highlighted the research projects of more than 40 fellows. This year, in addition to the traditional poster session, the symposium featured an interactive poster session, in which fellows were assigned to small groups to present and/or listen to poster presentations on multidisciplinary topics. **Kristin Moy, Ph.D.**, a postdoctoral fellow in NEB, said, “The interactive poster session was a unique chance to present my work and to learn about other work going on in DCEG. I also enjoyed meeting and interacting with other fellows across the Division.”

Robert N. Hoover, M.D., Sc.D., Director of DCEG’s Epidemiology and Biostatistics Program, closed the day by speaking about understudied areas within the Division and offered advice on how fellows can become involved



Andrew Freedman, Faith Davis, and Robert Hoover.

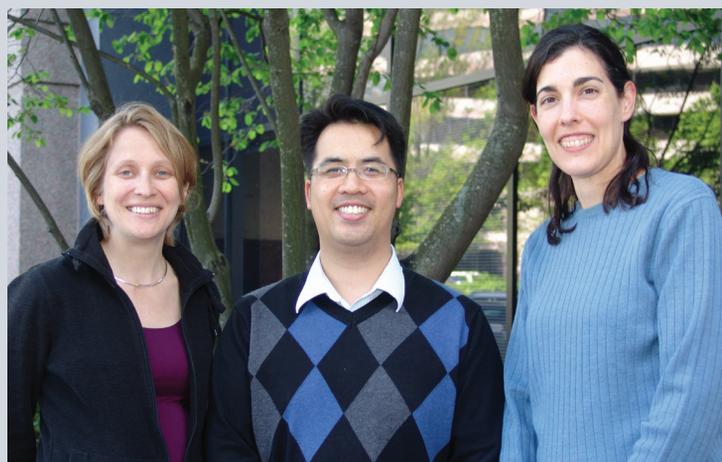
and grow beyond their current focus. Dr. Hoover captured the essence of the day in his closing comments: “There are uncharted territories all around us; your

charge is to use the tools available within the Division to explore them.” ■

—Hannah Arem, M.H.S., and Patricia Luhn, Ph.D., M.P.H.

NEW REPRESENTATIVES FOR FELLOWS COMMITTEES

Postdoctoral fellows **Gabriel Lai, Ph.D.**, Nutritional Epidemiology Branch (NEB), and **Christina Persson, Ph.D.**, Hormonal and Reproductive Epidemiology Branch (HREB), have been selected to serve as cochairs for the DCEG Fellows (DFel) Committee in 2012. They will take over from **Jacqueline Major, Ph.D.** (NEB), and **Britton Trabert, Ph.D.** (HREB).



Christina Persson, Gabriel Lai, and Clara Bodelon.

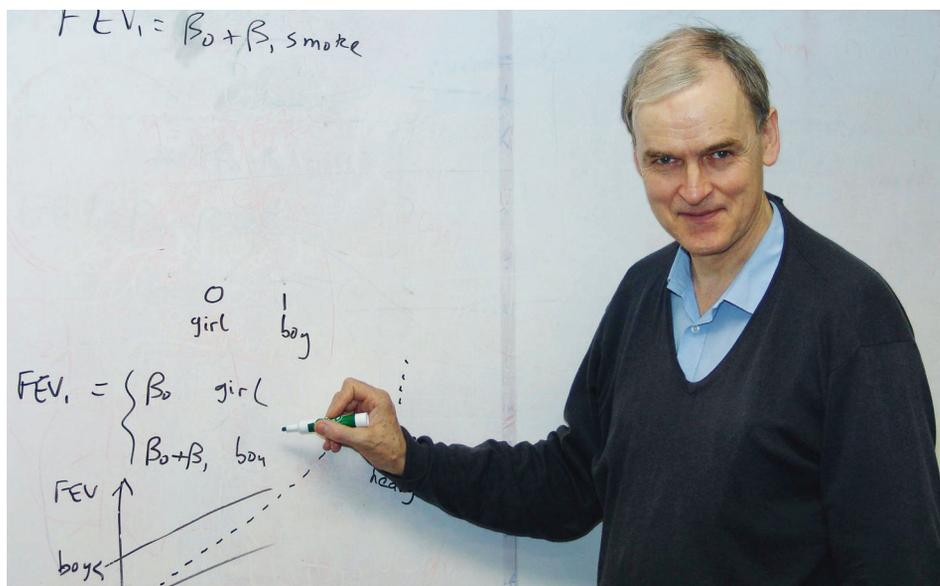
DFel was organized in early 2011 to enhance the intramural training experience of fellows within the Division. DFel meetings are open to all DCEG fellows and are scheduled for the fourth Wednesday of every month.

Clara Bodelon, Ph.D., M.S., postdoctoral fellow in HREB, will serve as DCEG’s new representative to the NIH Fellows Committee (FelCom) for the coming year. She is replacing **Phoebe Lee, Ph.D.**, Laboratory of Translational Genomics, and **Alison Mondul, Ph.D.** (NEB). FelCom enhances communication among fellows across the NIH community and serves as a liaison to research training programs that affect the fellowship experience. More information about FelCom is available at <http://felcom.od.nih.gov>.

MARK LITTLE PRESENTS A COURSE ON LINEAR MODELING

Mark Little, Ph.D., a senior investigator in the Radiation Epidemiology Branch (REB), gave a series of classes on “Introduction to Linear Models” to an enthusiastic group of DCEG staff members, including fellows, investigators, and scientific support staff. The classes covered mathematical theory and R analytic software features related to linear modeling.

Dr. Little, who came to DCEG from the United Kingdom, studied mathematics at Trinity College, Cambridge University, and obtained his doctorate in mathematics at New College, Oxford University. Dr. Little has been analyzing dose-response relationships for cancer and cardiovascular disease risks in various irradiated populations. He also has developed mechanistic models of carcinogenesis and cardiovascular disease in populations exposed to ionizing radiation and cigarette smoke.



Mark Little

Dr. Little originally set out to mentor an REB fellow on analysis, but he decided to make the course available to the entire Division. The topics that Dr. Little has covered have included linear models, linear model fitting, linear model

diagnostics, linear model building and checking, generalized linear models, Poisson models, logistic models, binomial models, and model building and regression diagnostics. ■

—Wendy Schneider-Levinson

DCEG PARTICIPATES IN ISBER ANNUAL MEETING

On May 15 to 18, the International Society for Biological and Environmental Repositories (ISBER) held its 13th annual meeting in Vancouver, Canada. The meeting’s theme was Keeping Step in an Evolving Global Research Environment: Biobanking for Now and for the Future, and it featured plenary sessions, educational and corporate workshops, contributed papers, poster sessions, and working group discussions.

ISBER is the leading international forum for addressing the technical, legal, ethical, and managerial issues relevant to repositories of biologic and environmental specimens. DCEG is one of the founding organizations of ISBER,

and several DCEG staff members play key roles in the society.

Marianne K. Henderson, M.S., Chief of the Office of Division Operations and Analysis, served as the 2011 to 2012 President of ISBER and was a Program Committee cochair for this year’s meeting. Ms. Henderson led off the meeting by speaking about ISBER’s recent achievements and activities on the horizon for 2013. She also served as chair of the annual awards presentation and business meeting.

Karen E. Pitt, Ph.D., special assistant for biological resources in DCEG’s Human Genetics Program, co-leads an effort to establish a certification

program for repository technicians as part of the ISBER Education and Training Committee. At the meeting, Dr. Pitt hosted an interactive discussion on the certification program development and planning activities.

As part of DCEG’s active biospecimen management, Ms. Henderson and Dr. Pitt coauthored two posters at the meeting. Dr. Pitt spoke on “An innovative approach to biospecimen storage that conserves energy and facility space,” and support contractor Ms. Kathleen Groover of Fisher BioServices, Inc., presented “Development and application of creative tools to accomplish rapid transfer of specimens from traditional freezers into a dense storage configuration.”

—Marianne K. Henderson, M.S.

ANN HSING RETIRES FROM NCI

Ann W. Hsing, Ph.D., retired in December 2011 from the Infections and Immunoepidemiology Branch (IIB) after 22 years with NCI. Dr. Hsing is a leading expert in the epidemiology and etiology of prostate and biliary tract cancers and has extensive experience with molecular epidemiology and with population-based studies in international settings.

Dr. Hsing received an M.P.H. in biostatistics from the University of California, Los Angeles, in 1981 and a Ph.D. in epidemiology from the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, in 1988. She conducted postdoctoral research at Johns Hopkins before joining NCI in 1989 as a cancer epidemiology and biostatistics fellow. Later, she was appointed as a tenure-track investigator and then a tenured investigator within DCEG.

Dr. Hsing spent seven years with the Biostatistics Branch, 12 years with the Hormonal and Reproductive Epidemiology Branch (HREB), and two years with IIB, during which time she developed an interdisciplinary research program to investigate the determinants of hormone-related cancers, particularly of the prostate and biliary tract. She conducted prostate cancer studies in the United States, China, and Ghana, using biomarker and genomic approaches to clarify the roles of hormonal, metabolic, and inflammatory mechanisms in prostate cancer etiology. She also helped lead the DCEG effort in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial for several years. Dr. Hsing's Shanghai Biliary Tract Cancer Study is the largest

population-based multidisciplinary study of this tumor to date and has yielded important etiologic leads.

Dr. Hsing has served on a number of committees and advisory boards, including the Biological Specimen Advisory Board of the American Cancer Society, the epidemiology committee of the International Consortium for Urologic Diseases, the U.S. Department of Defense's Center for Prostate Disease Research, and the Editorial Board of *Cancer Epidemiology, Biomarkers & Prevention*. She also has served as an adjunct professor in the Department of Epidemiology and the Department of Urology at the George Washington University in Washington, D.C.

While at NCI, Dr. Hsing received numerous accolades for her research and mentoring, including NIH Merit Awards for her work on prostate and biliary tract cancers, a DCEG Outstanding Mentor Award, and an award for promoting research quality as the chair of the DCEG Technical Evaluation of Protocols Committee. She also served as a DCEG



Ann Hsing

Prior to her retirement from NCI, Dr. Hsing transitioned her studies to investigators in both IIB and HREB, with whom she will continue to collaborate. Dr. Hsing has assumed the position of Director of Research at the Cancer Prevention Institute of California (CPIC) in Fremont, along with an appointment as full member of the Stanford Cancer Institute and professor at Stanford University in Palo Alto, California. At CPIC and Stanford, she will integrate information from her studies of cancer etiology and health disparities to develop an effective cancer prevention model for the Bay Area's multiethnic population. ■

—Victoria A. Fisher, M.P.H.

Women Scientist Advisor for several years and received recognition for her leadership and achievement.

Prior to her retirement

JUN-MO NAM HONORED WITH KSEA AWARD

Jun-mo Nam, M.S., of the Biostatistics Branch, was honored by the Korean-American Scientists and Engineers Association (KSEA) in 2011 with the prestigious Outstanding Contribution to KSEA Award. The award was presented by the Republic of Korea's Minister of Education, Science, and Technology at the annual U.S.-Korea Conference on Science, Technology, and Entrepreneurship in Park City, Utah. The award recognized Mr. Nam's lifetime accomplishments in biostatistics and his sustained outstanding contributions to the development of KSEA over 30 years. Established as a professional organization in 1971, KSEA helps provide career development opportunities among Korean-American scientists and engineers while fostering international cooperation between Korea and the United States.



Jun-mo Nam

SCIENTIFIC HIGHLIGHTS

ALL CANCERS

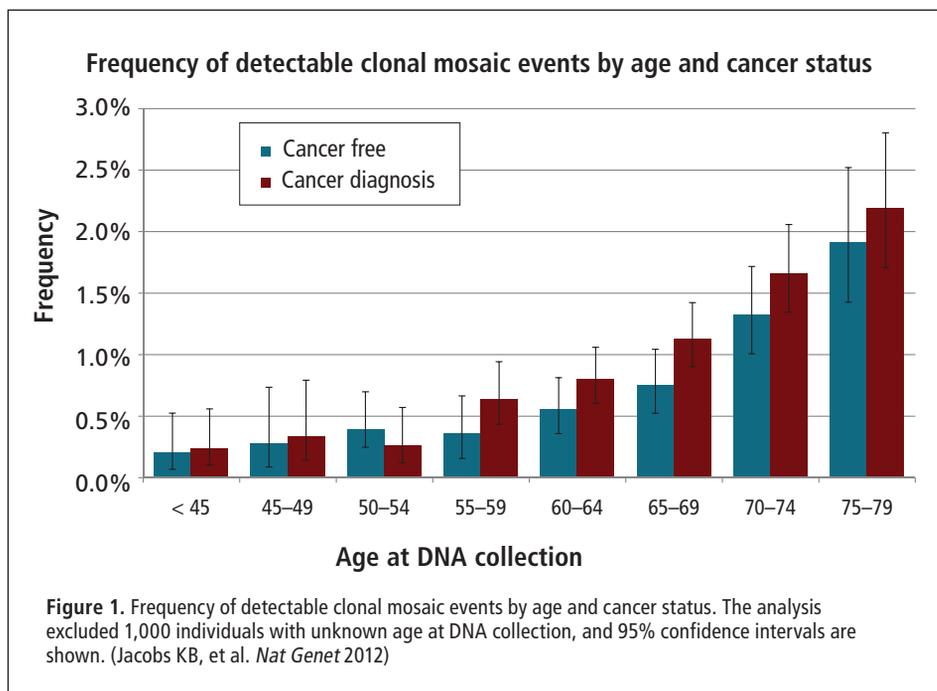
Clonal Mosaicism, Aging, and Cancer

In an analysis of 31,717 cancer cases and 26,136 cancer-free controls from 13 GWAS, the authors observed large chromosomal abnormalities in a subset of clones in DNA obtained from blood or buccal samples. Mosaic abnormalities, either aneuploidy (an abnormal number of chromosomes) or loss of heterozygosity (diversity in genes and possible loss of the normal function of a gene due to mutations), larger than 2 megabases were observed in non-sex chromosomes of 517 individuals (0.89%). In cancer-free individuals, frequency increased with age (see Figure 1), from 0.23% at under 50 years to 1.91% between 75 and 79 years ($p = 4.8 \times 10^{-8}$). Mosaic abnormalities were more common in individuals with solid tumors (0.97% versus 0.74% in cancer-free individuals; OR = 1.25). Detectable mosaicism also was more common in individuals from whom DNA was collected at least one year before leukemia diagnosis than in cancer-free individuals (OR = 35.4). These findings underscore the time-dependent nature of somatic events in the etiology of cancer and potentially other late-onset diseases. (Jacobs KB, Yeager M, Zhou W, et al. Detectable clonal mosaicism and its relationship to aging and cancer. *Nat Genet* 2012; May 6 [E-pub ahead of print])

ALL-CAUSE MORTALITY

Coffee Drinking

The investigators examined the association of coffee drinking with subsequent total and cause-specific mortality among 229,119 men and 173,141 women in the NIH-AARP Diet and Health Study who were 50–71 years of age at baseline. Participants with cancer, heart disease, and stroke were excluded. During



follow-up between 1995 and 2008, a total of 33,731 men and 18,784 women died. In age-adjusted models, the risk of death was increased among coffee drinkers. However, coffee drinkers were more likely to smoke, and after adjustment for tobacco-smoking status and other potential confounders, there was a significant inverse association between coffee consumption and mortality. Adjusted HRs for death among men who drank coffee compared with those who did not were as follows: 0.99 for drinking less than one cup per day, 0.94 for one cup, 0.90 for two or three cups, 0.88 for four or five cups, and 0.90 for six or more cups of coffee per day; the respective HRs among women were 1.01, 0.95, 0.87, 0.84, and 0.85. Inverse associations were observed for deaths due to heart disease, respiratory disease, stroke, injuries and accidents, diabetes, and infections, but not for deaths due to cancer. (Freedman ND, Park Y, Abnet CC, et al. Association of coffee drinking with total and cause-specific mortality. *N Engl J Med* 2012;366:1891–1904)

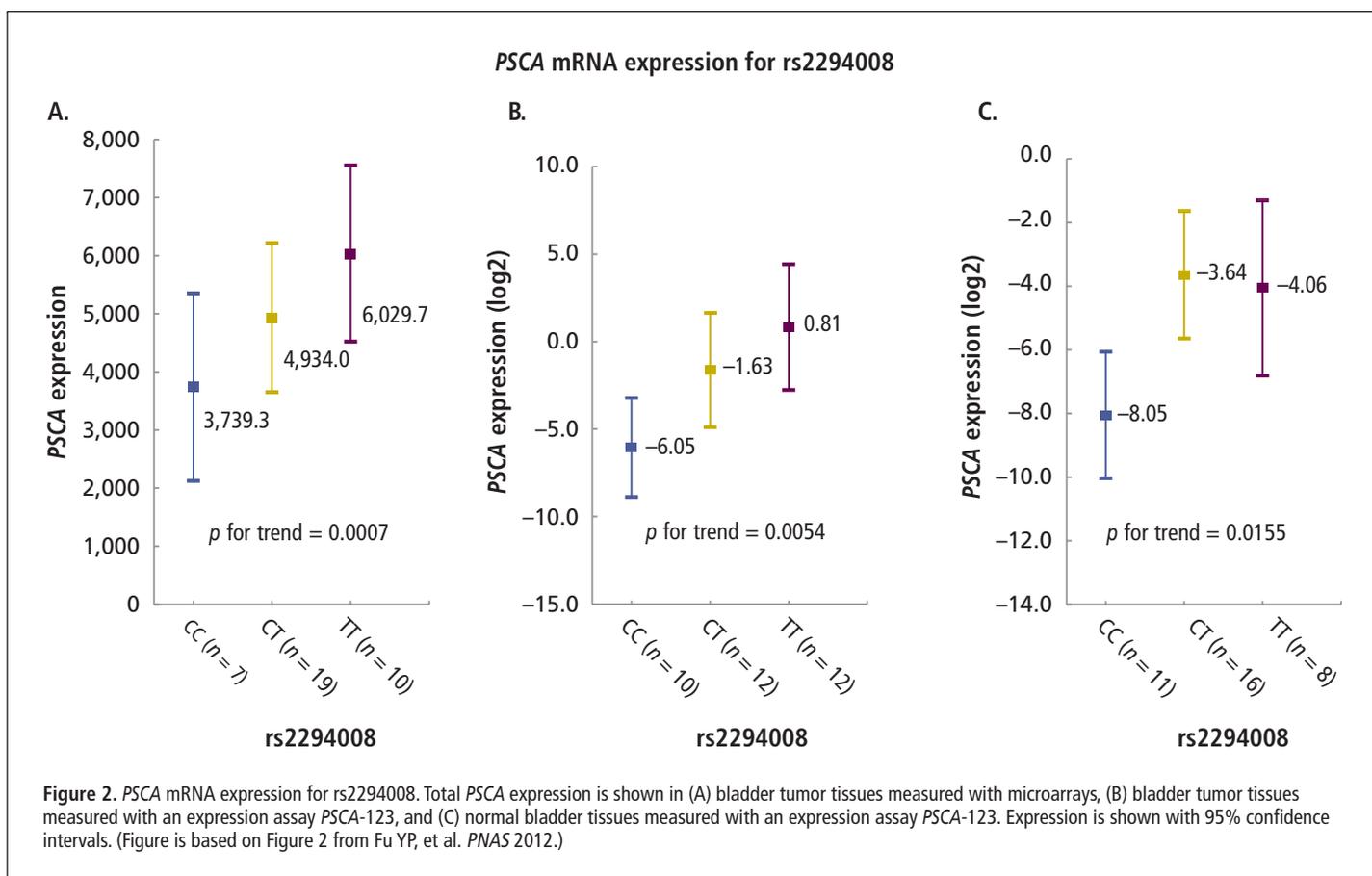
Sedentary Behaviors

In a follow-up study of 240,819 adults in the NIH-AARP Diet and Health Study, the authors found that higher amounts of sitting time and television viewing were associated with mortality, even after adjustment for age, sex, education, smoking, diet, race, and moderate-vigorous physical activity (MVPA). Compared with participants who reported viewing television for less than one hour daily, participants

GLOSSARY

GWAS	Genome-wide association study/studies
HPV	Human papillomavirus
HR	Hazard ratio
mRNA	Messenger RNA
OR	Odds ratio
SNP	Single nucleotide polymorphism

Note: This glossary defines acronyms that occur in more than one summary throughout the Scientific Highlights section.



who reported viewing television seven or more hours daily were at greater risk of all-cause (HR = 1.61), cardiovascular (HR = 1.85), and cancer (HR = 1.22) mortality after adjustment for MVPA. Overall sitting time was associated with all-cause mortality. Even for adults reporting more than seven hours per week of MVPA, high television viewing time remained associated with increased risk of all-cause (HR = 1.47) and cardiovascular (HR = 2.00) mortality. (Matthews CE, George SM, Moore SC, et al. Amount of time spent in sedentary behaviors and cause-specific mortality in US adults. *Am J Clin Nutr* 2012;95:437–445)

BLADDER CANCER

Genetic Variants in the PSCA Gene GWAS have identified a SNP, rs2294008, on 8q24.3 within the prostate stem cell antigen (*PSCA*) gene as a risk factor for bladder cancer. To fine map this region, the authors imputed 642 SNPs within

100 kilobases of rs2294008 and 33 markers genotyped in one of the reported GWAS in 8,652 subjects. A multivariable logistic regression model adjusted for rs2294008 revealed a unique signal, rs2978974. In the combined analysis of 5,393 cases and 7,324 controls, the authors detected a per-allele OR of 1.11 for rs2294008 and 1.07 for rs2978974. The effect was stronger in carriers of both risk variants (OR = 1.24), and there was a significant multiplicative interaction ($p = 0.035$) between these two SNPs, which requires replication in future studies. The T risk allele of rs2294008 was associated with increased *PSCA* mRNA expression in two sets of bladder tumor samples and in normal bladder samples (see Figure 2), but rs2978974 was not associated with *PSCA* expression. A joint effect of two *PSCA* SNPs, rs2294008 and rs2978974, suggests that both variants may be important for bladder cancer

susceptibility, possibly through different mechanisms that influence the control of mRNA expression and interaction with regulatory factors. (Fu YP, Kohaar I, Rothman N, et al. Common genetic variants in the *PSCA* gene influence gene expression and bladder cancer risk. *Proc Natl Acad Sci USA* 2012;109:4974–4979)

Mapping of the UGT1A Locus Identifies Protective Variant

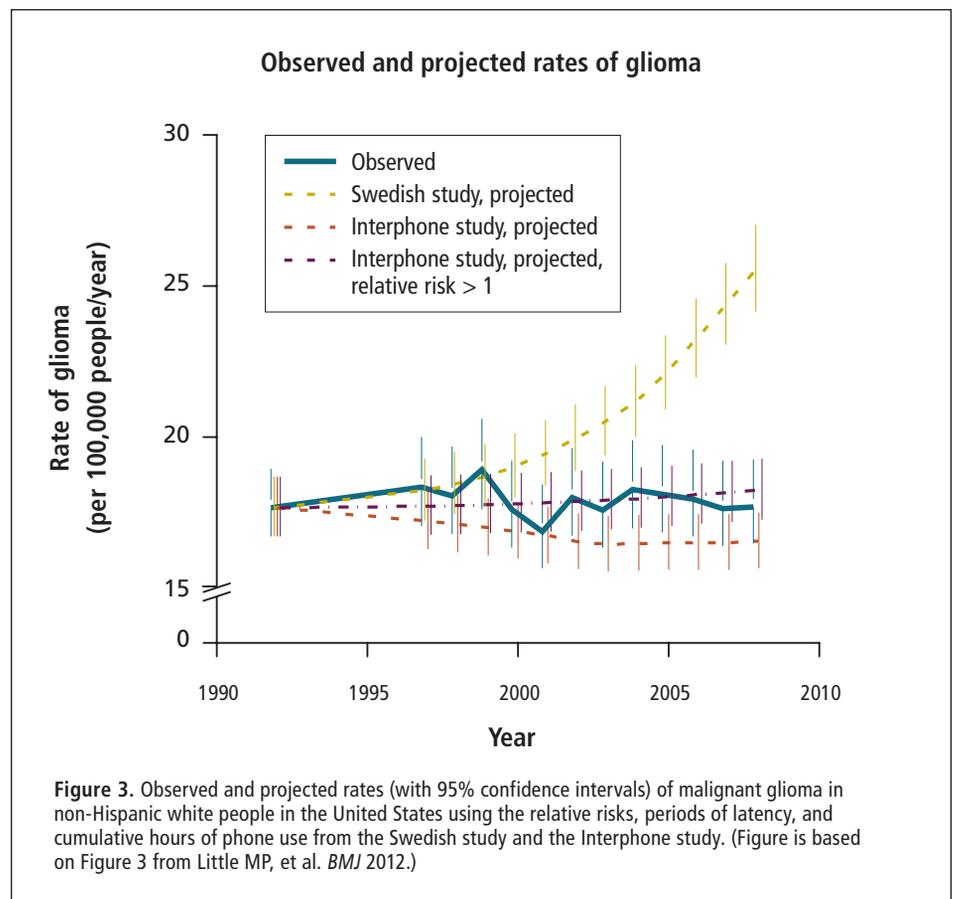
A recent GWAS of bladder cancer identified the *UGT1A* gene cluster on chromosome 2q37.1 as a novel susceptibility locus. The association within the *UGT1A* locus was detected by the SNP rs11892031. The authors performed detailed resequencing, imputation, and genotyping in this region, clarifying the original genetic association detected by rs11892031 and identifying an uncommon SNP, rs17863783, that explained and strengthened the association in this region. The authors found the protective

T allele of rs17863783 to be associated with increased mRNA expression of UGT1A6.1 both *in vitro* and in human liver tissue samples. Rs17863783 may protect from bladder cancer by increasing the removal of carcinogens from bladder epithelium by the UGT1A6.1 protein. (Tang W, Fu YP, Figueroa JD, et al. Mapping of the *UGT1A* locus identifies an uncommon coding variant that affects mRNA expression and protects from bladder cancer. *Hum Mol Genet* 2012;21:1918–1930)

BRAIN CANCER

Mobile Phone Use and Glioma Risk

In view of mobile phone exposure's classification as a possible human carcinogen by the International Agency for Research on Cancer, the authors compared the observed U.S. incidence trends for glioma (a form of brain cancer) with expected rates based on risks reported in two European studies. Projected rates were estimated by combining relative risks reported in the 2010 Interphone study and a 2011 Swedish study with U.S. population data from the Surveillance, Epidemiology and End Results program. Age-specific incidence rates of glioma in the U.S. remained generally constant from 1992 to 2008 (−0.02% change per year), a period coinciding with a substantial increase in mobile phone use. Based on relative risks of glioma by tumor latency and cumulative hours of phone use in the Swedish study, predicted U.S. rates should have been at least 40% higher than observed rates in 2008 (see Figure 3). The authors determined that increased risks of glioma with mobile phone use, as reported by the Swedish study, are inconsistent with observed incidence trends in U.S. population data, although the U.S. data could be consistent with the modest excess risks reported in the Interphone study. (Little MP, Rajaraman P, Curtis RE, et al. Mobile phone use and glioma risk: Comparison of epidemiological study results with incidence trends in the United States. *BMJ* 2012;344:e1147)



BREAST CANCER

Estrogen Metabolism

The authors evaluated the influence of estrogen metabolism in a case-control study of breast cancer nested in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. Participants included 277 women who developed invasive breast cancer and 423 matched control subjects; all were aged 55–74 years, postmenopausal, and not using hormone therapy at PLCO baseline. Liquid chromatography-tandem mass spectrometry was used to measure baseline serum concentrations of 15 estrogens and metabolites. Most estrogens, estrogen metabolites, and metabolic pathway groups were associated with increased breast cancer risk; the serum concentration of unconjugated estradiol was strongly associated (HR = 2.07). No estrogen, estrogen metabolite, or metabolic pathway group

remained significantly associated with breast cancer risk after adjusting for unconjugated estradiol. The ratio of the 2-hydroxylation pathway to parent estrogens (HR = 0.66) and the ratio of 4-hydroxylation pathway catechols to 4-hydroxylation pathway methylated catechols (HR = 1.34) were associated with breast cancer risk. More extensive 2-hydroxylation of parent estrogens was associated with lower risk, and less extensive methylation of potentially genotoxic 4-hydroxylation pathway catechols was associated with higher risk. (Fuhrman BJ, Schairer C, Gail MH, et al. Estrogen metabolism and risk of breast cancer in postmenopausal women. *J Natl Cancer Inst* 2012;104:326–339)

Fine Mapping of 14q24.1

In the Cancer Genetic Markers of Susceptibility (CGEMS) GWAS, a SNP marker, rs999737, in the 14q24.1 interval was associated with breast cancer risk.

To fine map this region, the authors imputed a 3.93 megabase region flanking rs999737 for stages 1 and 2 of the CGEMS study (5,692 cases, 5,576 controls) using the combined reference panels of the HapMap 3 and the 1000 Genomes Project. They performed single-marker association testing and variable-sized sliding window haplotype analysis. For both analyses, the initial tagging SNP rs999737 retained the strongest association with breast cancer risk. Investigation of contiguous regions did not reveal evidence for an additional independent signal. The authors concluded that rs999737 is an optimal tag SNP for common variants in the 14q24.1 region, thereby reducing the number of candidate variants that should be investigated in follow-up evaluation. (Lee P, Fu YP, Figueroa JD, et al. Fine mapping of 14q24.1 breast cancer susceptibility locus. *Hum Genet* 2012;131:479–490)

Risk for Hispanic Women

The authors evaluated the use of the Breast Cancer Risk Assessment Tool (BCRAT) for Hispanic women. The model, which estimates a woman's risk of developing invasive breast cancer over a defined period of time given her age and risk factor profile, combined 1990–1996 breast cancer incidence for Hispanic women with relative risks for breast cancer risk factors from non-Hispanic white women. The authors compared the relative risks and calibration of BCRAT risk projections of 6,353 Hispanic and 128,976 non-Hispanic white postmenopausal participants aged 50 and older in the Women's Health Initiative (WHI). Calibration was assessed by the ratio of the number of breast cancers observed (O) to the number expected (E) by the BCRAT (O/E). The authors re-evaluated calibration for an updated BCRAT that combined BCRAT relative risks with 1993–2007 breast cancer incidence,

which is contemporaneous with the WHI. In the WHI Main Study, the BCRAT underestimated the number of breast cancers by 18% in both Hispanics (O/E = 1.18) and non-Hispanic whites (O/E = 1.18). Updating the BCRAT improved calibration for Hispanic women (O/E = 1.08) and non-Hispanic white women (O/E = 0.98). For Hispanic women, relative risks for number of breast biopsies (1.71 vs. 1.27) and age at first birth (0.97 vs. 1.24) differed between the WHI and BCRAT. The modest discriminatory accuracy of the BCRAT for Hispanic women might be improved by using risk factor relative risks specific to Hispanic women. (Banegas MP, Gail MH, LaCroix A, et al. Evaluating breast cancer risk projections for Hispanic women. *Breast Cancer Res Treat* 2012;132:347–353)

CERVICAL CANCER

HPV Infection, Cytologic Abnormalities, and Co-testing

The authors assessed the longitudinal relationship of abnormal cytology and HPV positivity in a seven-year prospective study of 2,500 women in Guanacaste, Costa Rica. At each semiannual or annual visit, cervical specimens were screened using liquid-based cytology and tested for more than 40 HPV types using MY09/MY11 L1 degenerate primer polymerase chain reaction-based methods. Based on previous work, the authors separated prevalent and newly detected infections in younger and older women. Among newly detected HPV-positive or cytology-positive events, HPV and cytology appeared together 58.2% of the time; when discordant, HPV tended to appear before cytology in younger and older women. Combining newly detected and prevalent events, HPV and cytology disappeared at the same time more than 70% of the time. When discordant, HPV tended to disappear

after cytology in younger and older women. Detection of HPV DNA and associated cytological abnormalities tend to begin and end together. However, when discordant, detection of HPV DNA tends to precede and/or last longer than associated cytologic abnormalities. (Markt SC, Rodriguez AC, Burk RD, et al. Longitudinal analysis of carcinogenic human papillomavirus infection and associated cytologic abnormalities in the Guanacaste Natural History Study: Looking ahead to cotesting. *J Infect Dis* 2012;205:498–505)

Methylation of HPV 16 Genome

Previous studies have suggested an association between HPV 16 genome methylation and both cervical intraepithelial neoplasia (CIN) 3 and cancer, but the results have been inconsistent. The authors designed a nested case-control study within a large prospective cohort of women who underwent multiple screenings for cervical cancer in Guanacaste, Costa Rica. The authors collected diagnostic specimens at the time of CIN 3 diagnosis and persistent HPV 16 infection, prediagnostic specimens at the first HPV 16–positive screening visit, and control specimens from women with infection clearance within two years. Increased methylation in diagnostic vs. control specimens at nine CpG sites, or regions of DNA where a cytosine nucleotide occurs next to a guanine nucleotide, was associated with an increased risk of CIN 3 and persistence. High methylation at three of these CpG sites was associated with a much higher risk when combined compared with low methylation at these sites (OR = 52). In this HPV 16–infected cohort, increased methylation of CpG sites within the HPV 16 genome before diagnosis and at the time of diagnosis was associated with cervical precancer. (Mirabello L, Sun C, Ghosh A, et al. Methylation of human papillomavirus type 16 genome and risk of cervical precancer in a Costa Rican population. *J Natl Cancer Inst* 2012;104:556–565)

ESOPHAGEAL CANCER

Genotypic Variants at 2q33

The authors conducted a meta-analysis of susceptibility loci that showed nominally significant p values in two previously published genome-wide scans of esophageal squamous cell carcinoma. The meta-analysis revealed five SNPs at 2q33 with $p < 5 \times 10^{-8}$, and the strongest signal was for rs13016963 (combined OR = 1.29, $p = 7.63 \times 10^{-10}$). An imputation analysis of 4,304 SNPs at 2q33 suggested a single association signal, and the strongest imputed SNP associations were similar to those from the genotyped SNPs. The authors conducted an ancestral recombination graph analysis to identify haplotypes that harbor the variants directly responsible for the detected association signal. This showed that the 5 SNPs exist in a single haplotype along with 45 imputed SNPs in strong linkage disequilibrium, and the strongest candidate was rs10201587, one of the genotyped SNPs. The meta-analysis found genome-wide significant SNPs at 2q33 that map to the *CASP8/ALS2CR12/TRAK2* gene region. Future studies of esophageal and other cancers should focus on comprehensive sequencing of this 2q33 locus and functional analysis of rs13016963, rs10201587, and other strongly correlated variants. (Abnet CC, Wang Z, Song X, et al. Genotypic variants at 2q33 and risk of esophageal squamous cell carcinoma in China: A meta-analysis of genome-wide association studies. *Hum Mol Genet* 2012;21:2132–2141)

Non-steroidal Anti-inflammatory Drug Use

The authors pooled data from six population-based studies within the Barrett's and Esophageal Adenocarcinoma Consortium (BEACON) to evaluate the association between non-steroidal anti-inflammatory drug (NSAID) use and risks of esophageal adenocarcinoma (EAC) and esophagogastric junctional

adenocarcinoma (EGJA). Compared with nonusers, individuals who had used NSAIDs had a reduced risk of EAC (OR = 0.68) and possibly of EGJA (OR = 0.83). Similar reductions were observed among individuals who took aspirin and those who took non-aspirin NSAIDs. Daily or more frequent NSAID use and 10 or more years of use showed ORs of 0.56 and 0.63, respectively, for EAC risk. Although reverse causation could partly explain the inverse association between NSAID use and EAC risk, these results suggest a possible role for NSAIDs in prevention of EAC and EGJA. (Liao LM, Vaughan TL, Corley DA, et al. Nonsteroidal anti-inflammatory drug use reduces risk of adenocarcinomas of the esophagus and esophagogastric junction in a pooled analysis. *Gastroenterology* 2012;142:442–452)

EYE CANCER

Family History and Second Cancer Risk

Investigators evaluated the risk of second cancer in a retrospective cohort of 1,852 retinoblastoma (RB) survivors of at least one year, classifying the *RB1* germline mutation, inherited or *de novo*, by inference from laterality of RB and positive family history. In bilateral survivors, the investigators found a relative risk (RR) of 1.37 for second cancers associated with a family history of RB, adjusted for treatment, age, and length of follow-up. The risk for melanoma was significantly elevated for survivors with a family history of RB (RR = 3.08), but the risk for soft tissue and bone sarcomas was not. The cumulative incidence of second cancers 50 years after diagnosis of bilateral RB, with adjustment for competing risk of death, was significantly higher for survivors with a family history (47%) than survivors without a family history (38%). (Kleinerman RA, Yu CL, Little MP, et al. Variation of second cancer risk by family history of retinoblastoma among long-term survivors. *J Clin Oncol* 2012;30:950–957)

GASTRIC CANCER

Effects of *Helicobacter pylori*, Garlic, and Vitamins

In an extension of the Shandong Intervention Trial to 14.7 years of follow-up, two weeks of antibiotic treatment for *Helicobacter pylori* (*H. pylori*) reduced the prevalence of precancerous gastric lesions, whereas 7.3 years of oral supplementation with garlic extract and oil (garlic treatment) or vitamin C, vitamin E, and selenium (vitamin treatment) did not. In this masked factorial placebo-controlled trial of 3,365 randomly assigned subjects, gastric cancer was diagnosed in 3.0% of subjects who received *H. pylori* treatment and in 4.6% of those who received placebo (OR = 0.61). Gastric cancer deaths occurred among 1.5% of subjects assigned *H. pylori* treatment and among 2.1% of those assigned placebo (HR of death = 0.67). Garlic and vitamin treatments were associated with non-significant reductions in gastric cancer incidence and mortality. In this high-risk population, short-term antibiotic treatment significantly reduced the incidence of gastric cancer by 39% over 15 years of follow-up. (Ma JL, Zhang L, Brown LM, et al. Fifteen-year effects of *Helicobacter pylori*, garlic, and vitamin treatments on gastric cancer incidence and mortality. *J Natl Cancer Inst* 2012;104:488–492)

LUNG CANCER

Body Mass Index and Smoking

The authors prospectively examined the association between body mass index (BMI) and the risk of lung cancer among 448,732 men and women in the NIH-AARP Diet and Health Study. BMI was inversely associated with the risk of lung cancer among both men and women (BMI ≥ 35 vs. 22.5–24.99 kg/m²: HR = 0.81 and 0.73, respectively). The inverse association was restricted to current and former smokers and was stronger after

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adjustment for smoking. Among smokers, the inverse association persisted even after finely stratifying on smoking status, time since quitting smoking, and number of cigarettes smoked per day. Sensitivity analyses did not support the possibility that the inverse association was due to prevalent undiagnosed disease. Results suggest that a higher BMI is associated with a reduced risk of lung cancer among current and former smokers. (Smith L, Brinton LA, Spitz MR, et al. Body mass index and risk of lung cancer among never, former, and current smokers. *J Natl Cancer Inst* 2012;104:778–789)

Diesel Exhaust in Miners Case-control Study

See article on pages 1–3 of this issue of *Linkage*. (Silverman DT, Samanic CM, Lubin JH, et al. The Diesel Exhaust in Miners Study: A nested case-control study of lung cancer and diesel exhaust. *J Natl Cancer Inst* 2012; March 5 [E-pub ahead of print])

Diesel Exhaust in Miners Cohort Study

See article on pages 1–3 of this issue of *Linkage*. (Attfield MD, Schleiff PL, Lubin JH, et al. The Diesel Exhaust in Miners Study: A cohort mortality study with emphasis on lung cancer. *J Natl Cancer Inst* 2012; March 5 [E-pub ahead of print])

METHODS

Bayesian Model for Studying Gene-environment Interaction

Investigators developed an approach for analyzing how a gene or chromosomal region associated with a disease interacts with an established environment risk factor to influence the disease risk. The approach was based on a Bayesian model that uses a latent genetic profile variable to capture all of the genetic variation in the entire targeted region and allows the environment effect to vary across different genetic profile categories, rather than analyzing one genetic marker at a time.

Using data collected in the Environment and Genetics in Lung Cancer Etiology (EAGLE) study, investigators applied the Bayesian model to evaluate the joint effect of smoking intensity and genetic variants in the 15q25.1 region, which contains a cluster of nicotinic acetylcholine receptor genes and has been shown to be associated with both lung cancer and smoking behavior. Investigators found evidence for gene-environment interaction ($p = 0.016$), and the smoking effect appeared to be stronger in subjects with a genetic profile associated with a higher lung cancer risk. The conventional test of gene-environment interaction based on the single-marker approach is far from significant. (Yu K, Wacholder S, Wang Z, et al. A flexible Bayesian model for studying gene-environment interaction. *PLoS Genet* 2012;8:e1002482)

Testing Gene-environment Interaction

Several methods for screening for gene-environment interaction that address the issue of assuming gene-environment independence have recently been proposed. In this report, the authors present a comparative simulation study of power and type I error properties of three classes of procedures: (1) the standard one-step case-control method; (2) the case-only method that requires an assumption of gene-environment independence; and (3) a variety of hybrid methods that aim to gain power by exploiting the assumption of gene-environment independence but can protect against false positives when the independence assumption is violated. These analyses suggest that although the case-only method generally has maximum power, it can create substantial false positives in large-scale studies even when a small fraction of markers are associated with the exposure in the population. All of the hybrid methods

protect well against such false positives and can retain power advantages over standard case-control tests. For future genome-wide scans for gene-environment interactions, researchers can attain major power gain by using alternatives to standard case-control analysis. Whether a case-only scan or a hybrid method should be used depends on the strength and direction of gene-environment interaction and association, tolerance for false positives, and the nature of replication strategies. (Mukherjee B, Ahn J, Gruber SB, and Chatterjee N. Testing gene-environment interaction in large-scale case-control association studies: Possible choices and comparisons. *Am J Epidemiol* 2012;175:177–190)

OROPHARYNGEAL CANCER

Oral HPV Infection

HPV infection is the main cause of a subset of oropharyngeal squamous cell carcinoma. To determine the prevalence of oral HPV infection in the United States, a cross-sectional study was conducted as part of the National Health and Nutrition Examination Survey 2009–2010. Participants aged 14–69 provided a 30-second oral rinse and gargle with mouthwash. DNA purified from oral exfoliated cells was evaluated for detection of HPV types. Demographic and behavioral data were obtained by interview. The overall prevalence of oral HPV infection was 6.9%, and HPV 16 prevalence was 1.0%. Oral HPV infection followed a bimodal pattern for age with peak prevalence in individuals aged 30–34 years (7.3%) and 60–64 years (11.4%). Men had a higher prevalence than women for any oral HPV infection (10.1% vs. 3.6%; unadjusted prevalence ratio [PR] = 2.80). Infection was more common among those with a history of any type of sexual contact than those without (7.5% vs. 0.9%; PR = 8.69) and increased with number of sexual

partners and cigarettes smoked per day. Associations with age, sex, number of sexual partners, and current cigarettes smoked per day were independently associated with oral HPV infection in multivariable models. (Gillison ML, Broutian T, Pickard RK, et al. Prevalence of oral HPV infection in the United States, 2009–2010. *JAMA* 2012;307:693–703)

OVARIAN CANCER

BRCA1 and BRCA2 Mutations

Approximately 10% of women with invasive epithelial ovarian cancer (EOC) carry deleterious germline mutations in *BRCA1* or *BRCA2*. The authors conducted a pooled analysis of 26 observational studies of women with ovarian cancer to characterize the survival of *BRCA* carriers with EOC compared with noncarriers and to determine whether *BRCA1* and *BRCA2* carriers show similar survival patterns. The five-year overall survival was 36% for noncarriers, 44% for *BRCA1* carriers, and 52% for *BRCA2* carriers. After adjusting for study and year of diagnosis, *BRCA1* and *BRCA2* mutation carriers showed more favorable survival than noncarriers (for *BRCA1*: HR = 0.78; for *BRCA2*: HR = 0.61). These survival differences remained after additional adjustment for stage, grade, histology, and age at diagnosis (for *BRCA1*: HR = 0.73; for *BRCA2*: HR = 0.49). Among patients with invasive EOC, having a germline mutation in *BRCA1* or *BRCA2* was associated with improved five-year overall survival, and *BRCA2* carriers had the best prognosis. (Bolton KL, Chenevix-Trench G, Goh C, et al. Association between *BRCA1* and *BRCA2* mutations and survival in women with invasive epithelial ovarian cancer. *JAMA* 2012;307:382–390)

DCEG PEOPLE IN THE NEWS

In January, DCEG staff participated in the NCI Gene-Environment Think-Tank sponsored by the NCI Epidemiology and Genomics Research Program in the Division of Cancer Control and Population Sciences. **Christian C. Abnet, Ph.D., M.P.H.**, Nutritional Epidemiology Branch (NEB), spoke on “Esophageal and gastric cancer risk: GWAS results and the importance of alcohol consumption”; **Nilanjan Chatterjee, Ph.D.**, Chief of the Biostatistics Branch (BB), spoke on “Goals of gene-environment interaction studies in cancer epidemiology”; and **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, Occupational and Environmental Epidemiology Branch (OEEB), gave a short presentation on the state of the science for bladder cancer. Drs. Abnet, Chatterjee, and Rothman also participated in group discussion panels. In addition, Dr. Chatterjee and **Stephen J. Chanock, M.D.**, Chief of DCEG’s Laboratory of Translational Genomics and Director of the NCI Core Genotyping Facility, each served as a moderator of a group discussion.

Amy Berrington de González, D.Phil., Radiation Epidemiology Branch (REB), recently served on the National Academies’ National Research Council’s Committee for the Evaluation of Space Radiation Cancer Risk Model. The committee was tasked with reviewing the National Aeronautics and Space Administration’s revised model for estimating cancer risk to astronauts resulting from space radiation. The model provides the basis for occupational safety limits on flight length for astronauts.

In April, BB staff members participated in the Eastern North American Region/International Biometric Society 2012 spring meeting in Washington, D.C.

Nilanjan Chatterjee, Ph.D., Chief of BB, led a roundtable discussion on “The role of statisticians at the NIH.” **Mitchell H. Gail, M.D., Ph.D.**, spoke on “Using SEER data to develop models of absolute cancer risk.” **Hormuzd A. Katki, Ph.D.**, organized a session titled “Individualized risk prediction using joint models of longitudinal and survival data,” during which he presented “A joint model of cervical cancer, Pap smears, and HPV tests for use in developing cancer screening guidelines.” Dr. Katki also organized a Graduate Student and Recent Graduate Council invited session on “Careers in biostatistics.” **Stephanie Kovalchik, Ph.D.**, presented a contributed paper on “A general binomial regression model for estimating standardized risk differences from cohort data.” **Ruth M. Pfeiffer, Ph.D.**, gave an invited talk titled “On joint risk prediction.” Poster presentations were given by **Summer Seongmin Han, Ph.D.**, on “Testing for gene-environment and gene-gene interactions under monotonicity constraints”; **Ju-Hyun Park, Ph.D.**, on “Distribution of allele frequencies and effect sizes and their interrelationships for common genetic susceptibility variants”; and **Joshua Sampson, Ph.D.**, on “Selecting a statistical test to detect associations with groups of genetic variants: A user’s guide.”

In December, **Anil K. Chaturvedi, Ph.D.**, and **Aimée R. Kreimer, Ph.D.**, both of the Infections and Immunology Branch (IIB), spoke on oral human papillomavirus natural history at the Ohio State University Medical Center in Columbus.

In January, **Amanda J. Cross, Ph.D.** (NEB), spoke on “Colorectal cancer etiology: The hunt for dietary associations” at Howard University College of Medicine in Washington, D.C. In March, Dr. Cross

gave a talk on “Preventing colorectal cancer” at the George Washington University School of Medicine and Health Sciences in Washington, D.C. In April, she spoke on “Carnivores and cancer: Is it red, white or...processed?” as part of the Field of Nutrition Seminar series at Cornell University in Ithaca, New York.

In March, **Benjamin Emmanuel, M.P.H.** (IIB), gave a presentation titled “HIV-associated Burkitt lymphoma is more likely to be EBV-associated” at the 19th Conference on Retroviruses and Opportunistic Infections in Seattle, Washington.

In January, **Eric A. Engels, M.D., M.P.H.** (IIB), spoke on “Cancer risk in older solid organ transplant recipients” at the Association of Specialty Professors Workshop on Solid Organ Transplantation in Older Adults held in Arlington, Virginia.

In February, **Eric A. Engels, M.D., M.P.H.**, and **Sam M. Mbulaiteye, M.D.**, both of IIB, participated in a working group that met in Lyon, France, to consider polyomaviruses (SV40, BK, JC, and Merkel cell viruses) and malaria for an International Agency for Research on Cancer Monograph on the Evaluation of Carcinogenic Risks to Humans.

In March, **Roberto Flores, Ph.D., M.P.H.** (IIB), presented an abstract on “Effect of delayed freezing on microbial composition in human feces: Lessons for epidemiological studies” at the National Interagency Confederation for Biological Research Forum on Biostabilization in Frederick, Maryland. Also in March, **Rashmi Sinha, Ph.D.** (NEB), senior author on the abstract, presented the results of their research at the International Human Microbiome Congress, organized by the European

consortium MetaHIT, in Paris, France. Also at the Congress, **James J. Goedert, M.D.** (IIB), presented a talk on “Fecal microbial determinants of fecal and systemic estrogens.”

In March, **Melissa Friesen, Ph.D.** (OEEB), spoke on “Systematically combining job-exposure matrices and exposure measurements to improve the occupational exposure assessment in a population-based cohort” at the Department of Environmental and Occupational Health Sciences of the University of Washington School of Public Health in Seattle. Also in March, Dr. Friesen gave a presentation on “Inside the black box: Advances in exposure assessment methods in population-based studies” at the University of British Columbia School of Population and Public Health and at the British Columbia Cancer Agency, both of which are in Vancouver, Canada.

In January, **Mitchell H. Gail, M.D., Ph.D.** (BB), spoke about “Fifteen-year effects of *Helicobacter pylori* treatment and garlic and vitamin supplements on gastric cancer incidence and mortality” during grand rounds at the University of Pennsylvania Perelman School of Medicine in Philadelphia.

In December, **Alisa M. Goldstein, Ph.D.**, Genetic Epidemiology Branch (GEB), gave a presentation on “*BAP1* mutations: Key questions and future directions” at the Third Annual

Translational Cancer Medicine Symposium, Mesothelioma-Melanoma Cancer Syndrome: Gene-Environment Interaction, hosted by the University of Hawaii Cancer Center and The Queen’s Medical Center in Honolulu, Hawaii.

Asieh Golozar, M.D., M.P.H. (GEB), was selected to receive the 2012 Dorothy and Arthur Samet Award from the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. The department faculty presents the award to a student whose doctoral work makes a significant contribution to the field of epidemiology.

In January, **Mark H. Greene, M.D.**, Chief of the Clinical Genetics Branch (CGB), presented the “2012 status report on ovarian cancer screening strategies” at the Gynecologic Oncology Group 84th Semi-Annual Meeting in San Diego, California.

In November, **Marianne K. Henderson, M.S.**, Chief of the Office of Division Operations and Analysis and current President of the International Society for Biological and Environmental Repositories (ISBER), and **Karen E. Pitt, Ph.D.**, special assistant for biological resources in DCEG’s Human Genetics Program (HGP), gave presentations at the first meeting of the European, Middle Eastern, and African Society for Biopreservation and Biobanking in Marseille, France.

In January, **Allan Hildesheim, Ph.D.**, Chief of IIB, spoke on “Efficacy of HPV vaccination against the stringent endpoints” at the Human Papillomavirus Vaccinations: Safety, Sound Efficacy, and Public Health Effectiveness Symposium in Helsinki, Finland. Also at the meeting, **Sholom Wacholder, Ph.D.** (BB), gave a presentation on “Safety of the HPV vaccination based on active adverse effect reporting.”

In April, **Lauren Houghton, M.Sc.**, a predoctoral fellow in the Epidemiology and Biostatistics Program, attended the 37th Annual Meeting of the Human Biology Association (HBA) in Portland, Oregon, and received the E.E. Hunt Student Prize for “an exceptional student presentation at the 2012 HBA Meeting.” Dr. Houghton spoke on “The timing of adrenarche among Bangladeshi and British youth.”

In March, **Terrence (Terry) Lee, M.P.H.** (REB), was selected to receive the Charlotte Silverman Award from the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. The award recognizes epidemiology doctoral students and newer faculty for outreach projects involving significant research, education, and/or service.

In March, **Shih-Wen (Wenny) Lin, Ph.D., M.P.H.** (NEB), gave a guest lecture on “Introduction to infectious diseases” as part of an introductory public health course at the University of Delaware in Newark.

In January, **Jacqueline Major, Ph.D.** (NEB), gave an invited talk on “Effect of the built environment on risk of prostate cancer” at the University of Pennsylvania’s Center for Clinical Epidemiology and Biostatistics in Philadelphia.

HIGHLY CITED DCEG PAPER

The American Association for Cancer Research recently announced in its journal *Clinical Cancer Research* that the paper “MicroRNA expression differentiates histology and predicts survival of lung cancer,” which was written by several DCEG scientists, was one of the most highly cited articles published in the journal in 2010. **Maria Teresa Landi, M.D., Ph.D.**, Genetic Epidemiology Branch (GEB), was lead author of the paper. Other authors included **Neil E. Caporaso, M.D.**, Chief of GEB; **Alisa M. Goldstein, Ph.D.** (GEB); **Jill Koshiol, Ph.D.**, Infections and Immunoepidemiology Branch; **Melissa Rotunno, Ph.D.** (GEB); and **Margaret A. Tucker, M.D.**, Director of DCEG’s Human Genetics Program.

In March, **Sam M. Mbulaiteye, M.D.** (IIB), gave a seminar on “Endemic, sporadic, and AIDS-related Burkitt lymphoma: Epidemiological patterns may be clues to molecular heterogeneity” at Duke University in Durham, North Carolina.

In December, **Alison Mondul, Ph.D.** (NEB), gave an invited talk on “The epidemiology of micronutrients and cancer” at the Uniformed Services University of the Health Sciences in Bethesda, Maryland.

In April, **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (OEEB), was the lead scientific speaker for a workshop on Biological Factors that Underlie Individual Susceptibility to Environmental Stressors and Their Implications for Decision-making, hosted by the National Academies in Washington, D.C. His presentation was titled “Characterization of the problem: What do we know about individual variability and its contribution to disease?”

In February, **Sharon A. Savage, M.D.** (CGB), spoke on “Telomeres in inherited disorders and cancer etiology: How short is too short?” at pediatric grand rounds and on “Advances in understanding dyskeratosis congenita and related telomere biology disorders” at hematology grand rounds at the New York Medical College in Valhalla. In March, Dr. Savage gave an invited presentation on “Bone marrow failure and telomere dysfunction syndromes: When to initiate a genetics evaluation” as part of a short course in cancer genetics offered at the 2012 Annual Clinical Genetics Meeting of the American College of Medical Genetics and Genomics in Charlotte, North Carolina. In April, she spoke on “Dyskeratosis congenita: A disorder of telomere biology” at a plenary session of the European Group for Blood and Marrow Transplantation’s 12th annual meeting in Geneva, Switzerland.

In March, **Mark Schiffman, M.D., M.P.H.** (CGB), presented as part of a session on the “Best hot topic papers from cancer epidemiology, biomarkers, and prevention” at the American Society of Preventive Oncology meeting in Washington, D.C. The title of his presentation was “A long-term prospective study of type-specific human papillomavirus infection and risk of cervical neoplasia among 20,000 women in the Portland Kaiser Cohort Study.”

In January, **Mark E. Sherman, M.D.**, Hormonal and Reproductive Epidemiology Branch (HREB), participated in the American Cancer Society Expert Roundtable on Integrating Pathological Materials into Epidemiologic Studies held in Atlanta, Georgia. In March, Dr. Sherman was appointed to the Scientific Advisory Board of the Avon Foundation for Women. Also in January, Dr. Sherman gave a lecture titled “Towards reducing cancer mortality among women: Why pathogenesis matters” at a Mayo Clinic Oncology Conference in Rochester, Minnesota. At the same meeting, **Nicolas Wentzensen, M.D., Ph.D.** (HREB), spoke on “DNA methylation analysis of gynecological cancers: Assessing etiologic heterogeneity and early detection.”

In January, **Steven L. Simon, Ph.D.** (REB), gave an invited lecture on “The NCI studies on radiation doses and cancer risks in the Marshall Islands associated with exposure to radioactive fallout” at the 17th Hiroshima International Symposium on Lessons from Unhappy Events in the History of Nuclear Power Development, held at the University of Hiroshima in Japan. In March, Dr. Simon spoke on “Response of the U.S. Department of Health and Human Services in protecting civilian American citizens in Japan during the Fukushima Daiichi incident” at the Military Medical Operations Symposium

on the U.S. Response to the Fukushima Daiichi Incident held at the Armed Forces Radiobiology Research Institute at the Uniformed Services University of the Health Sciences in Bethesda, Maryland.

In December, **Rashmi Sinha, Ph.D.** (NEB), led a dietary working group and presented meat and chronic disease mortality analyses at the Asia Cohort Consortium meeting in Dhaka, Bangladesh. Also in December, she gave an invited lecture on “Meat, coffee intake, and colorectal cancer” at the Fourth International Conference on Translational Cancer Research: Recent Developments in Cancer Prevention in Udaipur, India. Dr. Sinha also gave presentations on diet and cancer at the Department of Epidemiology at the University of Texas MD Anderson Cancer Center in Houston in January and at the International Agency for Research on Cancer in Lyon, France, in March.

In December, **Philip R. Taylor, M.D., Sc.D.** (GEB), spoke on “Chemoprevention of cancer” at a course on fundamentals of clinical oncology for public health practitioners at Johns Hopkins University in Baltimore, Maryland.

In December, **Margaret A. Tucker, M.D.**, Director of HGP, spoke on the “Potential health risks associated with tanning beds” at the Nuclear and Radiation Studies Board of the National Academies in Washington, D.C.

In March, **Nicolas Wentzensen, M.D., Ph.D.** (HREB), participated in a debate session at the 2012 American Society for Colposcopy and Cervical Pathology Biennial Meeting in San Francisco, California. He presented the view that random biopsies should not be the standard of care for colposcopy.

COMINGS...GOINGS



Bari Ballew

Bari Ballew, Ph.D., joined the Clinical Genetics Branch (CGB) as a postdoctoral fellow. She received her Ph.D. in biology from

the University of California, San Diego, where her doctoral dissertation focused on the regulation of DNA end processing at telomeres and at DNA double-strand breaks. She will work with **Sharon A. Savage, M.D.** (CGB), in the telomere molecular epidemiology research program. Dr. Ballew's projects will target various aspects of disease susceptibility

in patients with dyskeratosis congenita, an inherited cancer predisposition syndrome caused by germline mutations in telomere biology genes, and new cancer gene discovery in DCEG's whole exome sequencing initiative.

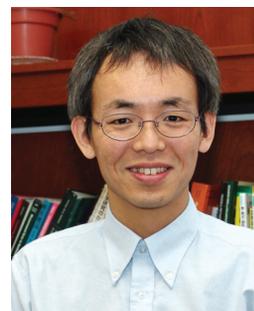


Kathleen Bern

Kathleen Bern joined the Administrative Resource Center as an administrative officer (AO). She previously worked at the NCI Division

of Cancer Treatment and Diagnosis and has more than 10 years of experience

as an AO. Ms. Bern will take over administrative duties for the Infections and Immunoepidemiology Branch and the Genetic Epidemiology Branch (GEB).



Kazutaka Doi

Kazutaka Doi, Ph.D., joined the Radiation Epidemiology Branch (REB) as a guest researcher from the National Institute of Radiological

Sciences in Chiba, Japan. Dr. Doi received his M.S. and Ph.D. in health science from the University of Tokyo Graduate School of Medicine in Japan. In REB, he will assess the impact of radiation dose uncertainty on thyroid cancer risk in two Chernobyl studies as well as undertake a dose-response analysis in the U.S. Radiologic Technologists Cohort Study. Dr. Doi will work with **Mark Little, Ph.D.** (REB); **Kiyohiko Mabuchi, M.D., Dr.P.H.**, Deputy Branch Chief of REB; and **Steven L. Simon, Ph.D.** (REB).

H. Dean Hosgood, III, Ph.D., left the Occupational and Environmental Epidemiology Branch (OEEB) for a position as assistant professor in the Division of Epidemiology at the Albert Einstein College of Medicine in New York, New York.

Zeina Khodr, Ph.D., joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a postdoctoral fellow. She received an M.S. in human genetics and an M.P.H. in

NEW LEADERSHIP FOR THE DCEG PROMOTION AND TENURE REVIEW PANEL

In January, **Patricia Hartge, Sc.D.**, Deputy Director of DCEG's Epidemiology and Biostatistics Program, was appointed chair of the DCEG Promotion and Tenure Review Panel (PTRP). She replaced outgoing chair **Shelia Hoar Zahm, Sc.D.**, scientific advisor (contractor) in DCEG's Office of the Director. **Catherine B. McClave, M.S.**, Chief of the Office of Communications and Special Initiatives, serves as PTRP's executive secretary.



Patricia Hartge and Catherine McClave.

Members of PTRP review scientific appointments and promotions at the GS-13 level (or equivalent) and above. The purview of PTRP extends to proposed promotions to tenure, as well as the quadrennial review of staff scientists and staff clinicians, prior to review at the NCI and NIH levels. In addition to Dr. Hartge and Ms. McClave, the current PTRP members include **Lynn R. Goldin, Ph.D.**, Deputy Chief of the Genetic Epidemiology Branch; **Barry I. Graubard, Ph.D.**, Biostatistics Branch; **Charles S. Rabkin, M.D.**, Infections and Immunoepidemiology Branch; and **Debra T. Silverman, Sc.D.**, Chief of the Occupational and Environmental Epidemiology Branch.



Zeina Khodr

epidemiology from Tulane University in New Orleans, Louisiana, and a Ph.D. in epidemiology from the University of Texas Health

Science Center at Houston School of Public Health. Her doctoral research focused on two areas of birth defects prevention: (1) the relationship between Hispanic acculturation and gastroschisis and (2) predictors for preconceptional folic acid supplementation. Dr. Khodr will work with **Jonine D. Figueroa, Ph.D., M.P.H.** (HREB), and **Gretchen L. Gierach, Ph.D.** (HREB), to study the molecular epidemiology of breast cancer.

Christian Kratz, M.D., left CGB for a tenured appointment as professor and department head of Pediatric Hematology/Oncology at the Hannover Medical School Children's Hospital in Hannover, Germany. While at CGB, Dr. Kratz's major research interests included familial testicular cancer, childhood cancer predisposition syndromes, inherited bone marrow failure syndromes, childhood myelodysplastic/myeloproliferative disorders, and developmental diseases caused by germline mutations in cancer-related genes. Dr. Kratz will continue to serve as an adjunct investigator in CGB.

Wenqing Li, Ph.D., joined GEB as a visiting postdoctoral fellow. He received his Ph.D. in epidemiology and biostatistics from Peking University in China. Dr. Li's doctoral dissertation involved studying gene-environment interactions in the evolution of precancerous



Wenqing Li

gastric lesions as well as the genetic factors that determine the effect of chemotherapy intervention trials. Since August 2011, Dr. Li has

worked as a postdoctoral research fellow at Brigham and Women's Hospital, Harvard Medical School, in Boston, Massachusetts, where he has studied risk factors and comorbidities of skin cancer and skin diseases. Under the mentorship of GEB senior investigators **Alisa M. Goldstein, Ph.D.**, and **Philip R. Taylor, M.D., Sc.D.**, Dr. Li will conduct research on genetic and environmental factors involved in the development of cancer.



Jiansong Ren

Jiansong Ren, Ph.D., M.P.H., joined the Nutritional Epidemiology Branch (NEB) as a visiting fellow. He received his Ph.D. in epidemiology and health statistics from Peking Union

Medical College in Beijing, China, where his dissertation focused on the association between serum pepsinogens, gastrin-17, and upper digestive tract cancers. Dr. Ren will work with **Christian C. Abnet, Ph.D., M.P.H.** (NEB), on etiologic studies of upper gastrointestinal tract cancers, including studies of B vitamins, sex hormones, and pepsinogens.



Jo Stenehjem

Jo Stenehjem, M.S., joined OEEB as a special volunteer. Mr. Stenehjem received his M.S. in epidemiology from the Norwegian University of

Science and Technology in Trondheim. He currently is pursuing a joint doctoral degree in epidemiology from the University of Oslo in Norway and the Cancer Registry of Norway, where he is a research fellow. He will work with OEEB senior investigators **Qing Lan, M.D., Ph.D., M.P.H.**, and **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, on a study of benzene-induced lymphohematopoietic cancers among Norwegian offshore oil industry workers.

LINKAGE WEB VERSION WINS SOCIETY FOR TECHNICAL COMMUNICATION AWARD

In February, the redesigned web version of *DCEG Linkage* earned an Excellence Award from the Washington, D.C., chapter of the Society for Technical Communication. The award recognizes excellence in content organization and scope, visual elements, navigation, accessibility, and writing and editing. DCEG staff members honored by the award include **Victoria A. Fisher, M.P.H.**, *Linkage* editor in the Office of Communications and Special Initiatives (OCSI), and **Wendy Schneider-Levinson**, *Linkage* managing editor in OCSI. *Linkage* contributors from Palladian Partners, Inc., also were recognized, including Ms. Maureen Berg, senior graphic designer; Ms. Sam Fox, senior web developer; and Ms. Elaine Garber, senior editor.

FIRST ARTHUR SCHATZKIN LECTURE IN NUTRITIONAL EPIDEMIOLOGY

In April, the first Arthur Schatzkin Distinguished Lecture in Nutritional Epidemiology was held in the NIH Clinical Center's Lipsett Amphitheater. NCI's Division of Cancer Control and Population Sciences (DCCPS), the NCI Division of Cancer Prevention (DCP), and DCEG established this annual lecture to honor the memory of Arthur Schatzkin, M.D., Dr.P.H., a visionary scientist, mentor, and leader in the field of nutrition and cancer.

The inaugural lecture was given by Dr. John Potter, member and senior advisor at the Fred Hutchinson Cancer Research Center (FHCRC) and professor of epidemiology at the University of Washington in Seattle. The title of his lecture was "Nutrition, environment, development, and cancer: Casting a wider net."

As a member and former director of the FHCRC Public Health Sciences Division, Dr. Potter focuses his research on the role of diet, physical activity, hormones, and genetics in the development of cancer, with an emphasis on the epidemiology, biology, early detection, and prevention of colon cancer. He has paid particular attention to the aspects of diet and physical activity that reduce risk—notably plant foods and the many



Arthur Schatzkin Distinguished Lecture organizing committee with speaker: (left to right) Rachel Ballard-Barbash (DCCPS), Yikyung Park (NEB), Victor Kipnis (DCP), Rashmi Sinha (NEB), John Potter (speaker), and Amy Subar (DCCPS). (Photograph credit: Bill Branson)

compounds they contain that may act in one way or another to slow or reverse the process of carcinogenesis.

Dr. Potter earned an M.B.B.S. in 1971 and a Ph.D. in epidemiology in 1984, both from the University of Queensland in Brisbane, Australia.

DCEG Director **Joseph F. Fraumeni, Jr., M.D.**, commented, "This annual lecture series affords us the opportunity to honor Arthur's memory and his seminal contributions to the field of nutritional epidemiology as well as provide a forum at NIH to discuss the

emerging research and concepts that are accelerating progress in the field."

Dr. Arthur Schatzkin joined NCI in 1984 and served as the Chief of the Nutritional Epidemiology Branch (NEB) in DCEG from 1995 to 2011. He was committed to understanding the role of nutrition in cancer etiology and prevention as well as developing new methods and resources to advance research in nutritional epidemiology. In addition, he was dedicated to training, mentoring, and supporting young scientists. Dr. Schatzkin passed away from cancer in January 2011. ■



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