

Linkage

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DCEG Studies in Africa: Seeking to Understand Cancer Causes on Another Continent

The investigation of global cancer incidence and mortality patterns can provide clues to cancer etiology and inform the development of cancer control strategies. Among DCEG's many international research activities are its studies in Africa, which stand to contribute significantly to our understanding of cancer and its risk factors.

According to the World Health Organization, Africa's already huge cancer burden will increase in future years—the 681,000 new cases of cancer and 512,000 deaths reported in 2008 are estimated to grow to 1.6 million new cases and 1.2 million deaths annually by 2030.

Contributing to the situation are the large number of infection-related cancers among HIV/AIDS patients and the high costs of cancer treatment, which most African patients cannot afford.

Research on HIV-related Cancer

HIV/AIDS has been linked to increased risks of Kaposi sarcoma (KS), non-Hodgkin lymphoma, Hodgkin lymphoma, and cancers of the cervix, anus, liver, and lung.

Effects of HIV on cancer incidence, however, appear to vary in magnitude by geographic region. Less is known about the risk of HIV/AIDS-associated cancers in Africa than in the United States, even though Africa is home to more than two-thirds of the nearly 34 million people infected with HIV worldwide. Approximately 30 percent of cancers in Africa are thought to be attributable to



Map shows countries in Africa in which DCEG conducts or has conducted research.

DCEG *Linkage*

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infections, including HIV. The incidence of KS has been steadily climbing in parallel with the HIV epidemic in sub-Saharan Africa, and the incidence of lymphomas has increased in several countries, including Nigeria and Uganda.

Scientists in DCEG's Infections and Immunoepidemiology Branch (IIB) have

contributed important insights into the origins and mechanisms of HIV/AIDS-related cancers and the role of immunity and inflammation in cancer. One approach has been to link HIV/AIDS registries to cancer registries in both the United States and Africa.

IIB researchers **Sam M. Mbulaiteye, M.D.**, and **Eric A. Engels, M.D., M.P.H.**, implemented the first record-linkage study of AIDS and cancer registries in Africa in Kampala, Uganda. The study provided the first well-characterized data on cancer risk in a defined African HIV-infected population and confirmed the increased risks of AIDS-defining cancers, while also revealing greater risks of some non-AIDS-defining cancers, including Hodgkin lymphoma and conjunctival cancer. The risk of these latter tumors, although they are rare, was subsequently found to be elevated among persons with HIV/AIDS in the United States. "In a few years, we would like to go back to do another record-linkage study in Uganda," Dr. Mbulaiteye said, "to assess the effect of antiretroviral drugs, which have become more available in the region. It is important to see if the impact of treatment is similar in Africa as in other populations."



EMBLEM study community research assistant Patrick Okullu conducts a household census in Labour Lane Village in Gulu, Uganda.

Another IIB investigator, **Charles S. Rabkin, M.D.**, has studied AIDS-related KS to address unresolved questions on the genomic integrity of KS, specifically whether multiple tumors in individuals arise as clones from a single cell of origin. In Zambia, Dr. Rabkin and colleagues found that all KS tumors in a given patient shared the same inactivated X chromosome, suggesting that KS is a monoclonal cancer that tends to disperse across the body. This work paved the way for additional studies involving KS pathogenesis, including a study in Uganda conducted by Dr. Mbulaiteye that is continuing to examine the clonal properties of KS.

Current Research in Africa

Building upon their research program on HIV/AIDS-related cancer in Africa, DCEG researchers have branched out to study a variety of tumors that are reported to occur more frequently or, in the case of prostate cancer, less frequently in Africa than in western populations.

Burkitt Lymphoma

Burkitt lymphoma (BL) is the most common childhood tumor in Africa, and infections with malaria and Epstein-Barr virus at an early age are widely accepted risk factors for this disease.

Dr. Mbulaiteye, study manager **Benjamin Emmanuel, M.P.H.** (IIB), and colleagues are conducting a case-control study of BL in Uganda, Tanzania, and Kenya—known as the Epidemiology of Burkitt's Lymphoma in East-African Children and Minors (EMBLEM) study—to explore whether genetic resistance to malaria lowers risk of BL. Some individuals appear to be genetically protected against malaria and have only mild infections, whereas other individuals must receive treatment to survive the disease. “The EMBLEM study is using modern technologies to address questions about malaria and genetics,” Dr. Mbulaiteye said. Blood and tissue samples gathered as part of the EMBLEM study will provide a resource for future molecular studies that incorporate technologies such as tumor microarrays.

Less than one year into the study, the investigators are enrolling participants and have introduced activities and protocols in the field. Staff training is an important aspect of a successful epidemiological study, according to Dr. Mbulaiteye. “We have trained local technicians in one country, and they are training local staff from other sites; they really do a wonderful job,” he said.

Kaposi Sarcoma

KS is a major public health problem in Africa and was endemic in many sub-Saharan African countries before the AIDS epidemic. Infection with human herpesvirus-8 (HHV8) is necessary for KS to occur, but other factors, such as HIV infection, greatly increase the risk of the disease. HHV8 prevalence varies dramatically across Africa, suggesting that cofactors correlated with geographic or environmental characteristics may influence risk of infection with the virus.

Dr. Mbulaiteye and colleagues are conducting a study in a sickle cell disease clinic in Kampala, Uganda, to explore

transmission routes for HHV8. So far, investigators have found that HHV8 transmission in blood is inefficient, but it does occur. They have documented that levels of HHV8 are considerably higher in saliva than in blood, a finding that adds support to a mechanism of salivary transmission from mother to child or from child to child. Further studies are being conducted across Uganda to assess small-area variation of HHV8 and to identify socio-demographic and environmental risk factors for HHV8 and KS.

Esophageal Cancer

Esophageal cancer is the sixth leading cause of cancer deaths worldwide, with esophageal squamous cell carcinoma (ESCC) accounting for more than 80 percent of all deaths from this disease.

In Africa, ESCC has a strikingly uneven geographical distribution with higher concentrations in several areas, including western Kenya, a region in which the disease often strikes young people. **Christian C. Abnet, Ph.D., M.P.H.**, Nutritional Epidemiology Branch (NEB), and colleagues have established a pilot study at Tenwek Hospital in Bomet, Kenya, to assess the feasibility of conducting a case-control study with biosamples to explore a wide range of etiologic factors for ESCC in Africa.

Also at Tenwek Hospital, **Sanford M. Dawsey, M.D.** (NEB), and colleagues are conducting a study to understand



After a productive site visit, EMBLEM investigators Tobias Kinyera, Steven Reynolds, Martin Ogwang, Allan Hildesheim, Mike Mbaziira, Sam Mbulaiteye, and Julia Royall pause at St. Mary's Hospital Lacor in Gulu, Uganda.

the risk factors for (and prevalence of) esophageal squamous dysplasia (ESD), the precursor lesion of ESCC. The study will enroll and endoscope asymptomatic adults in the area to determine the prevalence of ESD. Dr. Dawsey will use the results to guide the design of programs to screen and treat ESD as well as studies that will compare risk factors for ESD and invasive ESCC among Kenyans.

Prostate Cancer

Prostate cancer incidence and mortality have long been thought to be lower among African men than among African American men, despite their similar genetic makeup. However, it was not known if this apparent discrepancy was due to differences in environmental factors or differences in the availability of screening, treatment, or reporting systems.

In 2001, **Ann W. Hsing, Ph.D.** (IIB), began a study to characterize the burden of prostate cancer in Ghana, a country in West Africa whose men are genetically closely related to African Americans, by using state-of-the-art screening protocols.



Staff training was conducted for the prostate cancer study in Ghana.

The team screened 1,038 randomly selected men for prostate cancer using both a digital rectal exam and the prostate-specific antigen test and then sent for biopsy those who screened positive. The biopsies revealed that 76 of the men had cancer, and those men were provided with treatment. The high prevalence rate suggested that Africans do not have a significantly lower occurrence of prostate cancer than African Americans. Dr. Hsing is continuing her research with a population-based, case-control study conducted in collaboration with the Korle-Bu Teaching Hospital, which is affiliated with the University of Ghana Medical School. Serum, plasma, and tissue samples from cases are being used in genome-wide association and other studies to better understand the genetic and other determinants of prostate cancer.

Breast Cancer

In Africa, breast cancer rates are rising, with a high frequency of cancers diagnosed at late stage and cancers that are either estrogen receptor negative (ER-) or triple negative (ER-, progesterone negative, and human epidermal growth factor receptor-2 negative). These

tumors tend to be aggressive and occur at younger ages. In addition, evidence indicates that inflammatory breast cancer (IBC), a rare, poorly understood, and particularly aggressive form of breast cancer, makes up a larger proportion of breast cancer cases in North Africa than in the United States. In North Africa, **Catherine Schairer, Ph.D.**, Biostatistics Branch, is conducting a case-control study in collaboration with the University of Michigan to investigate the causes of IBC. Study centers in Egypt, Tunisia, and Morocco are currently enrolling participants.

Louise A. Brinton, Ph.D., Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), and **Jonine D. Figueroa, Ph.D., M.P.H.** (HREB), are conducting a feasibility assessment for a multidisciplinary, case-control study of breast cancer in Ghana to determine why incidence rates of this malignancy are rising in western Africa. Dr. Brinton hopes to coordinate her initiative with ongoing efforts against breast cancer in Ghana and to use various partnerships to build the infrastructure for this study as well as future research activities in this country.

Laying Groundwork for the Future

DCEG scientists are helping to build the capacity for cancer research in Africa. Toward this end, it is essential to train African scientists to participate in collaborative research as well as to foster independent research efforts in Africa. DCEG's Africa Working Group was recently established by Drs. Abnet, Dawsey, Hsing, and Mbulaiteye to enhance communication across the Division and Institute and to suggest priorities for future collaborative research that will provide new etiologic insights into cancer in Africa while reducing its burden. ■

—Victoria A. McCallum, M.P.H.,
and Wendy Schneider-Levinson

DCEG STAFF ARE HONORED WITH NIH DIRECTOR'S AWARDS

In August, two staff members were honored with special recognition at the NIH Director's Award Ceremony. **Sanford M. Dawsey, M.D.**, a senior investigator in the Nutritional Epidemiology Branch, was awarded an NIH Ruth L. Kirschstein Mentoring Award for "exemplary performance while demonstrating significant leadership, skill, and ability in serving as a mentor." **Aaron E. Blair, Ph.D., M.P.H.**, a scientist emeritus in the Occupational and Environmental Epidemiology Branch, received two NIH Director's Awards for work performed with the National Institute of Environmental Health Sciences related to the 2010 Gulf of Mexico oil spill. The first award recognized the Deepwater Horizon Gulf Oil Spill Response Team for implementing public health protection programs for cleanup workers, developing an epidemiologic study, and assembling a research consortium. The second award recognized the Gulf Long-term Follow-up (GuLF) Study Team for rapidly developing a protocol for the GuLF Study and obtaining the necessary human subject protection clearances and other administrative requirements associated with longitudinal federal research studies.

DCEG RESEARCH HIGHLIGHTED AT THE CONGRESS OF EPIDEMIOLOGY

In June, DCEG members participated in the Third North American Congress of Epidemiology in Montreal, Canada, which was organized by five epidemiologic societies. This Congress convenes only once every five years and showcases the diversity of research, practice, and policy within the field of epidemiology.

DCEG staff members who participated in planning groups for the Congress included **Louise A. Brinton, Ph.D.**, Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), **Gretchen L. Gierach, Ph.D.** (HREB), **Patricia Hartge, Sc.D.**, Deputy Director of DCEG's Epidemiology and Biostatistics Program, and **Philip S. Rosenberg, Ph.D.**, of the Biostatistics Branch.

Over the course of the four-day meeting, DCEG scientists chaired symposia, gave invited and contributed talks, and presented posters. **Amy Berrington de González, D.Phil.**, Radiation Epidemiology Branch (REB), chaired a symposium on pediatric computed tomography (CT) screening titled "To scan or not to scan? The pediatric CT debate," where she presented her work on "Projected cancer risks from pediatric CT scans." Dr. Hartge moderated a session on "Breast cancer: Beyond the basics," at which Dr. Gierach discussed her work on the "Relationship of perilesional mammographic density to pathologic diagnosis." **Shih-Wen (Wenny) Lin, Ph.D., M.P.H.**, Nutritional Epidemiology Branch (NEB), chaired a session titled "Tissue-based immune markers of cancer." The session included a presentation from **Jill Koshiol, Ph.D.**, Infections and Immunoepidemiology Branch, who spoke on "Evaluating immune markers in epidemiologic studies."

Other DCEG participants included **Charles E. Matthews, Ph.D.** (NEB), who discussed his work on "The biological mechanisms underlying the links between sedentary behaviors and disease," and **Kathryn Hughes Barry, Ph.D.**, Occupational and Environmental Epidemiology Branch, who spoke on "Genetic variation in base excision repair pathway genes, pesticide exposure, and prostate cancer risk." In addition, **Preetha Rajaraman, Ph.D.** (REB), presented "Early-life exposure to diagnostic radiation and ultrasound scans and risk of childhood cancer."

Dr. Hartge and **Jennifer Loukissas, M.P.P.**, communications manager for DCEG's Office of Communications and Special Initiatives, coordinated a symposium titled "Communicating epidemiology: The changing landscape." At this session, Ms. Loukissas presented strategies for epidemiologists to communicate with the media.

Two DCEG Branch Chiefs gave presentations on career development. **Martha S. Linet, M.D., M.P.H.**, Chief of REB, spoke on government careers in epidemiology in the workshop "Career choices: Figure out where you want to work and how to get there." Dr. Brinton chaired a roundtable session on "Women in cancer research and career mentoring."

The Congress provided a special opportunity to recruit future trainees and to



Jackie Lavigne receives the Alexander D. Langmuir Award on behalf of DCEG from John Vena and Stanley Weiss at the Congress.

reconnect with former colleagues. **Jackie Lavigne, Ph.D., M.P.H.**, Chief of the Office of Education, and Ms. Loukissas met with interested graduate students at the DCEG fellowship booth. In addition, current DCEG fellows organized a happy hour for former fellows and research staff at a local eatery.

The Congress honored DCEG with the first Alexander D. Langmuir Award for Training Program Excellence and Innovation. This award recognizes an exceptional graduate training program with an emphasis on robust skill development in epidemiological principles and research (see the full article in the July 2011 issue of *Linkage*). In addition, Dr. Margaret Spitz, of The University of Texas MD Anderson Cancer Center in Houston and special advisor to DCEG, received the Abraham M. Lilienfeld Award for Overall Excellence in Epidemiology. ■

—Jennifer Loukissas, M.P.P.

JONINE FIGUEROA—A GREAT TIME TO BE A MOLECULAR EPIDEMIOLOGIST

When asked how she got into the field of molecular epidemiology, **Jonine D. Figueroa, Ph.D., M.P.H.**, Hormonal and Reproductive Epidemiology Branch (HREB), recalled, “I had just completed my Ph.D. in molecular genetics and cell biology, and I wanted something more applied. I heard about the NCI Cancer Prevention Fellowship Program, which allows you to get an M.P.H., and it sounded great.” She was accepted into the program in 2004 and went to Columbia University for her M.P.H. She now leverages her laboratory expertise to apply molecular techniques in epidemiologic studies in order to delineate the mechanisms involved in cancer causation and progression. She hopes that this work may lead to novel strategies for risk assessment and interventions.

At NCI, she found the ideal mentor in Dr. Montserrat García-Closas, then an investigator in HREB. “With her epidemiologic and analytic expertise plus my molecular biology background, she was the perfect fit for me,” Dr. Figueroa said. In 2008, Dr. Figueroa became a tenure-track investigator in the Division. Much of her initial work focused on bladder cancer as she applied her molecular background to define mechanisms of genetic susceptibility.

Dr. Figueroa later turned to breast cancer, focusing her efforts on identifying genetic and other risk markers, especially for aggressive and early-onset tumors. She recently published a pooled analysis on the association of common genetic variants at 1p11.2 and 14q24.1 (*RAD51L1*) with breast cancer risk and found evidence for heterogeneity by tumor subtype. These findings demonstrate the importance of conducting large studies incorporating tumor pathology data in order to provide the most robust

risk models for assessing predisposition to different types of breast cancer.

In further studies, Dr. Figueroa received an NCI Director’s Innovation Award to study the *TP53* pathway in estrogen receptor negative (ER–) breast cancer. She explained that most identified risk factors for breast cancer are related to estrogen receptor positive tumors, which account for about 70 percent of all breast cancers. On the other hand, ER– breast cancers have been relatively understudied despite being generally more aggressive and deadly and more frequent among younger women, *BRCA1* mutation carriers, and African Americans. ER– breast cancers are reported to have more *TP53* mutations, the reason for Dr. Figueroa’s interest in this pathway.

The theme of her current work is identifying biomarkers associated with early carcinogenic events in breast tissue. “Cancer arises at one end of the spectrum,” she explained, “but we have limited understanding of the initiating events that eventually progress to breast cancers. Biomarkers are a tool we can use to help us understand the biological mechanisms by which genetic and non-genetic factors increase or decrease the subsequent risk for breast cancer.”

To begin to answer this question, Dr. Figueroa is collaborating with researchers at the Susan G. Komen for the Cure Tissue Bank at Indiana University. The study population includes about 900 women volunteers, aged 18 to 83 years, who completed questionnaires and donated blood and breast tissue but who have no evidence of cancer. The goal is to look for associations between terminal ductal lobular unit (TDLU) morphology and genetic susceptibility loci as well as hormonal and other risk factors. TDLUs, which are milk-secreting structures, are

thought to be where the majority of breast cancers originate.

“Are risk factors associated with changes in the TDLU structure suggesting a pathway to

breast carcinogenesis? That’s the question we want to answer,” Dr. Figueroa explained. She and her colleagues are examining the samples of normal tissue for any sign of changing morphology, which scientists have previously shown to be an independent marker of risk in a study at the Mayo Clinic of high-risk women with benign breast disease. Tissues from the normal-tissue bank will make it possible to see whether changes occur earlier, before the onset of any disease.

“This is an exciting time to be a molecular epidemiologist because we have new technologies and population-based biological samples needed to more fully understand the molecular mechanisms leading to disease,” Dr. Figueroa said.

Dr. Figueroa confesses to being a “foodie”—she regularly cooks Puerto Rican dishes with her key ingredient: sofrito. She lives with her husband Jeff, a dog geneticist, their 1½-year-old daughter Isis, and a Leonberger dog named Zeppelin. “Being a wife, mother, and tenure-track researcher is challenging,” she admitted. “It has been a tough year in some ways, but I am very happy and I have fun. My motto is ‘Work Hard, Play Hard.’ I think it’s a good motto!” ■



Jonine Figueroa

GRETCHEN GIERACH EXPLORES THE ORIGINS OF BREAST CANCER

Hormonally related cancers in women have been a long-term interest for **Gretchen L. Gierach, Ph.D.**, who was appointed as a tenure-track investigator in the Hormonal and Reproductive Epidemiology Branch (HREB) in January 2010. Her interest in women's health began while she was an undergraduate student at Pennsylvania State University. After working for several years in the field of women's health research, she attended the University of Pittsburgh Graduate School of Public Health, where she received her M.P.H. and Ph.D. in epidemiology, with an emphasis in women's health and cancer epidemiology.

One of Dr. Gierach's graduate studies focused on mammographic density—that is, the tissue composition of the breast as reflected in a mammogram. High mammographic density is one of the strongest risk factors for breast cancer, and yet little is known about why. Dr. Gierach's work in mammographic density piqued her interest in defining density as an intermediate marker for studying breast cancer etiology.

When Dr. Gierach joined NCI in 2006 as a Cancer Prevention Fellow, HREB Branch Chief **Louise A. Brinton, Ph.D.**, offered her the opportunity to develop and oversee a new project known as the Breast Radiology Evaluation and Study of Tissues (BREAST), which is funded by proceeds from the sale of the U.S. Postal Service Breast Cancer Research Stamp. The study, which Dr. Gierach co-leads with **Mark E. Sherman, M.D.**, a senior clinician in HREB, considers both the radiologic features of the breast through mammography and the histologic, molecular, and biochemical characteristics of breast tissue among women undergoing image-guided breast biopsies at the University of Vermont

Breast Cancer Surveillance System site. Dr. Gierach is relating indices of mammographic density to tissue-level biomarkers that may uncover the mechanisms linking high mammographic density to breast cancer risk.

Dr. Gierach and colleagues are currently analyzing data from the BREAST Stamp Project with a focus on relating measures of density to serum levels of growth factors and estrogenic hormones. An exciting and novel aspect of this work is the development of new methods to measure density in specific regions of the breast, as opposed to the more traditional approach that uses a single measure for the entire breast. “This assessment allows us to study the morphologic heterogeneity of breast tissue in the context of epidemiologic risk factors,” Dr. Gierach explained. The ability to characterize breast density as a volume as opposed to a two-dimensional area may provide a more thorough and accurate representation of breast tissue composition.

In collaboration with the DCEG Clinical Genetics Branch, Dr. Gierach has reported that mammographic density is similar between cancer-free women with *BRCA1/2* mutations, which increase the risk of breast cancer, and women at low-to-average risk of developing breast cancer. This finding raises important questions about the use of mammographic density for risk prediction in women with *BRCA1/2* mutations.

Dr. Gierach is launching a new study with Dr. Sherman in Detroit, Michigan, that will use a new technology called ultrasound tomography to characterize changes in breast density, which are thought to correlate with changes in breast cancer risk. Ultrasound tomography measures the density of the entire

volume of the breast and does not involve ionizing radiation, thereby permitting researchers to safely take repeated measurements. Dr.



Gretchen Gierach

Gierach will use ultrasound tomography to define a time course of changes in breast density among women taking tamoxifen, which is known to reduce both breast density and breast cancer risk. This information will enable scientists to explore using breast density as a kind of “biosensor” of tamoxifen response and find out whether ultrasound tomography can be a useful tool in making this determination.

“If we demonstrate the utility of ultrasound tomography as a tool for measuring breast density changes in these participants,” Dr. Gierach said, “this study could be a launching point to investigate how specific changes in breast density relate to breast carcinogenesis.” Dr. Gierach also noted that the study population will be approximately 50 percent African American, a group that has been underrepresented in studies of breast density to date.

Dr. Gierach is obviously busy with her work at NCI, but she loves every minute of it. “Being able to collaborate with clinicians specializing in breast pathology has greatly enhanced my efforts,” she said. “I feel very fortunate to have DCEG colleagues whose research I have admired for so long.” ■

—Amber K. Boehm, Ph.D.

DCEG HOSTS VISITING SCHOLAR SCOTT DAVIS

DCEG welcomed Visiting Scholar Dr. Scott Davis in June. Dr.

Davis is chairman of the Department of Epidemiology at the University of Washington School of Public Health and a full member of the Fred Hutchinson Cancer Research Center. He is renowned for his contributions to understanding the biological effects of ionizing and non-ionizing radiation, the etiology of leukemias and lymphomas, and the health effects of circadian disruption.

Dr. Davis obtained his undergraduate degree in biology and chemistry from the University of New Mexico in Albuquerque, an M.S. in community health from the University of Rochester in New York, and a Ph.D. in epidemiology from the University of Washington in Seattle. Early in his career, he served as a research associate in epidemiology at the Radiation Effects Research Foundation in Hiroshima, Japan, and was a special fellow of the Leukemia Society of America. He is an elected member of the American Epidemiological Society and a fellow of the American College of Epidemiology. Dr. Davis is the only foreign epidemiologist to be elected a member (academician) of the Russian Academy of Medical Sciences.

For more than a decade, Dr. Davis has directed two major research programs investigating the effects of ionizing radiation on human health: (1) a series of studies in the Russian Federation on the effects of radiation exposure from the Chernobyl accident and (2) the Hanford Thyroid Disease Study, a long-term follow-up study of thyroid disease in persons exposed to atmospheric releases of radiation from the Hanford nuclear site in eastern Washington State. He also has conducted several epidemiologic



Shelia Hoar Zahm, Patricia Hartge, Lindsay Morton, Scott Davis, and Robert Hoover.

studies of the possible health effects of exposure to power frequency magnetic fields, focusing on the risk of leukemia and breast cancer. Recently, this work has expanded to include investigations of the effects of exposure to light at night and circadian disruption on melatonin and reproductive hormones in relation to the etiology of breast and other endocrine-related cancers.

Robert N. Hoover, M.D., Sc.D., Director of the Epidemiology and Biostatistics Program (EBP), welcomed Dr. Davis and applauded him for his collegial style and seminal contributions to the field of radiation epidemiology. Dr. Davis began his two-day visit with a seminar titled “Shift work as a probable carcinogen: Does working at night really increase cancer risk?” In his overview of evidence regarding night shift work and subsequent cancer risk, Dr. Davis described the progression of his investigations and possible future research directions.

First postulated by Dr. Richard Stevens of the University of Connecticut, the

“melatonin hypothesis” proposes that exposure to light at night may be a risk factor for breast cancer, particularly in westernized societies, through its ability to suppress nocturnal melatonin production by the pineal gland—with the result that estrogen is then not suppressed. One of the most effective and prevalent causes of exposure to light at night is working at night, and considerable evidence indicates that night shift workers experience a variety of adverse health effects.

Dr. Davis explained the challenges in defining shift work as an exposure and the wide variation across epidemiologic studies. One of his efforts, the Seattle Breast Cancer Study, was among the first to report an increased risk of breast cancer associated with exposure to light at night and shift work. Dr. Davis and his colleagues also have investigated the relationship of magnetic field exposure to nocturnal levels of melatonin and the effect of shift work on female hormone profiles. They will soon be conducting similar studies in male populations.

The International Agency for Research on Cancer recently classified shift work as a “probable human carcinogen,” based primarily on increased breast cancer risk among nurses, flight attendants, and others with work-related disruption of circadian patterns.

During his visit, Dr. Davis participated in several meetings with DCEG scientists. **Gretchen L. Gierach, Ph.D.**, Hormonal and Reproductive Epidemiology Branch, facilitated a session titled “Circadian disruption and hormone-related cancers.” The group posed questions on measuring stress biomarkers, how to define sleep and night-shift work, and possible DCEG studies that could investigate circadian rhythm and cancer risk.

Preetha Rajaraman, Ph.D., Radiation Epidemiology Branch (REB), led a discussion on “Environmental and occupational radiation exposures and cancer risks.” The session focused on new results in the field of radiation epidemiology, lessons learned from the recent nuclear disaster in Japan, and studies of susceptible groups for low-dose exposures.

Patricia Hartge, Sc.D., Deputy Director of EBP, **Martha S. Linet, M.D., M.P.H.**, Chief of REB, and **Jennifer Loukissas, M.P.P.**, Office of Communications and Special Initiatives, hosted a session titled “Communicating findings from epidemiologic studies on issues of major public concern.” Dr. Davis began a lively discussion with an overview of the many challenges that surrounded the Hanford Thyroid Disease Study, including the perceptions of the public and the media. He emphasized the need to develop messages and to be clear about what questions can and cannot be answered by a particular study. Dr. Davis also met with early-career scientists in DCEG for an informal brown bag luncheon to discuss various research topics and career planning.

“It is always inspiring to be here,” Dr. Davis said, citing the stimulating



Scott Davis

exchange of ideas and hospitality from DCEG investigators. He enthusiastically expressed his appreciation to DCEG for hosting him as a visiting scholar and stated, “I get more out of this visit than anyone else, and I always look forward to my return.” ■

—Victoria A. McCallum, M.P.H.

FORMALDEHYDE ADDED TO HUMAN CARCINOGEN LIST

In June, the National Toxicology Program of the National Institute of Environmental Health Sciences added formaldehyde to the list of known human carcinogens in the *Twelfth Report on Carcinogens*. This addition was based on epidemiologic evidence that higher exposure to formaldehyde increases the risk for nasopharyngeal cancer, sinonasal cancer, and myeloid leukemia.

Formaldehyde was first listed in the *Second Report on Carcinogens* in 1981 as “reasonably anticipated” to be a human carcinogen, based on positive studies in experimental animals. Since that time, epidemiologic and toxicologic studies of occupational groups have been reported by DCEG scientists, including Occupational and

Environmental Epidemiology Branch (OEEB) scientists **Laura Beane Freeman, Ph.D.**, **Aaron E. Blair, Ph.D., M.P.H.**, **Qing Lan, M.D., Ph.D., M.P.H.**, **Lee E. Moore, Ph.D.**, and **Nathaniel Rothman, M.D., M.P.H., M.H.S.**; former OEEB scientists Dr. Richard B. Hayes, Dr. Min Shen, Dr. Patricia Stewart, and Dr. Roel Vermeulen; Director of DCEG **Joseph F. Fraumeni, Jr., M.D.**; Director of the Epidemiology and Biostatistics Program **Robert N. Hoover, M.D., Sc.D.**; and former Biostatistics Branch scientists Dr. Michael Hauptmann and Dr. Jay H. Lubin.

Formaldehyde is a high-production chemical with a wide variety of uses. Exposure can occur in numerous industries and professions, such as manufacturing of formaldehyde and

formaldehyde-based resins, woodworking, and furniture making. Morticians, pathologists, and laboratory workers are commonly exposed to the chemical. The general population is also exposed to formaldehyde by breathing contaminated indoor or outdoor air and from tobacco smoke. Cleaning agents, glues, adhesives, salon products (such as hair coloring, smoothing, and straightening formulas), and other consumer goods may contain formaldehyde.

For detailed information on the *Twelfth Report on Carcinogens*, go to <http://go.usa.gov/8UW> (case sensitive).

—Victoria A. McCallum, M.P.H.

NIH RECOGNIZES 2012 FARE WINNERS

Ten DCEG scientists received NIH Fellows Awards for Research Excellence (FARE). This award recognizes scientific research by intramural postdoctoral fellows and by predoctoral fellows conducting their doctoral dissertation research at NIH. Winners receive a \$1,000 travel stipend to attend and present their work at a scientific meeting. This year's awardees, listed below along with the titles of their abstracts, represent seven DCEG branches.

Francesco Barone-Adesi, M.D., Ph.D., Occupational and Environmental Epidemiology Branch (OEEB): "Risk of lung cancer associated with domestic use of different types of coal in Xuanwei, China"

Kathryn Hughes Barry, Ph.D. (OEEB): "Genetic variation in DNA repair genes, pesticide exposure, and prostate cancer"

Clara Bodelon, Ph.D., M.S., Genetic Epidemiology Branch: "Immunogenetics and risk of mortality after lung cancer diagnosis"

Cher Dallal, Ph.D., Hormonal and Reproductive Epidemiology Branch (HREB): "Accelerometer-based measures of active and sedentary behaviors in relation to breast cancer risk"

Jonathan Hofmann, Ph.D. (OEEB): "Pre-existing kidney disorders and risk of renal cell carcinoma: Results from a population-based case-control study of Caucasians and African Americans"

Gabriel Lai, Ph.D., Nutritional Epidemiology Branch: "The association of diabetes with cancer incidence and mortality in the NIH-AARP Study"

Idan Menashe, Ph.D., formerly of the Biostatistics Branch: "Pathway-based analysis of a bladder cancer

genome-wide association study suggests involvement of cellular detoxification processes"

Gila Neta, Ph.D., M.P.P., Radiation Epidemiology Branch: "Variation in the risk of radiation-related breast cancer by histology and estrogen receptor expression"

Wei Tang, Ph.D., Laboratory of Translational Genomics: "Uncommon coding variants within the *UGT1A* cluster protect against bladder cancer through independent functional mechanisms"

Britton Trabert, Ph.D. (HREB): "Estrogen plus progestin menopausal hormone use: A safe regimen with respect to endometrial cancer risk?"

More information about the FARE competition is available at <http://go.usa.gov/9qW> (case sensitive). ■

BIostatistics STAFF RECOGNIZED AT JOINT STATISTICAL MEETINGS

Staff members of the Biostatistics Branch (BB) participated in and received several honors at this summer's 2011 Joint Statistical Meetings (JSM) in Miami Beach, Florida. JSM is an annual conference for statisticians with activities that include invited and contributed oral and poster presentations, panel and roundtable discussions, continuing education courses, and a career placement service.

Nilanjan Chatterjee, Ph.D., Chief of BB, was awarded the Committee of Presidents of Statistical Societies (COPSS) Presidents' Award (see article on page 11), and **Mitchell H. Gail, M.D., Ph.D.**, received the Nathan Mantel Lifetime Achievement Award for the development of statistical methods for epidemiology (see box on page 11). **Arpita Ghosh, Ph.D.**, received a Young Investigator Award from the Statistics in Epidemiology Section of the American Statistical

Association, which recognized her contribution as a lead author of the paper "Unified analysis of secondary phenotypes in case-control association studies."

Presentations, posters, and panel discussions made by BB staff at the meeting included the following:

Nilanjan Chatterjee, Ph.D.: "Predicting the future of genetic risk prediction"

Mitchell H. Gail, M.D., Ph.D.: "Risk-based preventive strategies: Improving risk models versus improving interventions" and "Comparative benefits for disease prevention of improved interventions versus more discriminating models of disease risk"

Barry I. Graubard, Ph.D.: "Estimating family aggregation of disease in cross-sectional surveys"

Summer Seongmin Han, Ph.D.: "Likelihood ratio test for detecting gene (G)-environment (E)

interactions under additive risk models exploiting G-E independence for case-control studies"

Stephanie Kovalchik, Ph.D.: "Does meta-regression have enough power? An empirical study of 500 meta-analyses of randomized controlled trials"

Victoria Landsman, Ph.D.: "Analysis of case-control studies with sample weights"

Ruth M. Pfeiffer, Ph.D.: "Two criteria for evaluating risk prediction models"

Joshua Sampson, Ph.D.: "Rare variants and searching for associations"

Jianxin Shi, Ph.D.: "Statistical analysis of copy number variations in family-based genome-wide association studies"

Sholom Wacholder, Ph.D.: "Personalized medicine and convergence: Prospects for statisticians"

NILANJAN CHATTERJEE RECEIVES PRESTIGIOUS STATISTICS AWARD

In August, **Nilanjan Chatterjee, Ph.D.**, Chief of the Biostatistics Branch (BB), was awarded the Committee of Presidents of Statistical Societies (COPSS) Presidents' Award at the 2011 Joint Statistical Meetings in Miami Beach, Florida. The award is presented annually to a person under the age of 41 in recognition of outstanding contributions to the profession of statistics.

First given in 1979, the COPSS Presidents' Award is generally recognized as the most prestigious award worldwide for early-career statisticians. The award is given by the five sponsoring societies: the American Statistical Association (ASA), Statistical Society of Canada, Institute of Mathematical Statistics, and the two North American Regions of the International Biometric Society.

Dr. Chatterjee is the first recipient outside of academia in the 32 years that the award has been given. He obtained his Ph.D. in statistics in 1999 from the University of Washington, Seattle. He then joined BB as a postdoctoral fellow and became a tenure-track investigator in 2001, a senior investigator in 2004, and Branch Chief in 2008.

Dr. Chatterjee is well-known for his groundbreaking research into increasing



Nilanjan Chatterjee receives the COPSS Presidents' Award from COPSS President Xihong Lin.

the efficiency of gene-environment and gene-gene interaction studies, assessing the future yield of modern genome-wide association studies (GWAS), and modeling subtype heterogeneity for complex diseases. He has made fundamental contributions to the analysis of case-control studies by developing new paradigms that exploit natural population genetic models for studies of genetic epidemiology. His research is grounded in many modern and classical aspects of statistics, including theory of biased sampling, missing data models, semiparametric inference, survival analysis, and shrinkage estimation techniques. He also

collaborates on a variety of epidemiologic studies, including recent GWAS that have contributed to a better understanding of the genetic basis of a variety of cancers. In addition, Dr. Chatterjee has published more than 175 articles, many of which appear in the top-tier journals of both statistics and genetics.

In 2008, he was elected to a fellowship in ASA, and in 2010, he received the Mortimer Spiegelman Award from the Statistics Section of the American Public Health Association. Earlier this year, Dr. Chatterjee received the Gertrude M. Cox Award from RTI International and the Washington Statistical Society for his outstanding scientific contributions as a young statistician. He was also selected to receive the COPSS George W. Snedecor Award, which is presented every two years to a statistician who has made distinguished contributions to the theory of biometry, including outstanding publications within three years of the date of the award. ■

—Wendy Schneider-Levinson

MITCHELL GAIL RECEIVES LIFETIME ACHIEVEMENT AWARD

In August, **Mitchell H. Gail, M.D., Ph.D.**, a senior investigator in the Biostatistics Branch, received the Nathan Mantel Lifetime Achievement Award for the development of novel statistical methods for epidemiology. The Statistics in Epidemiology Section of the American Statistical Association presented him with the award at the 2011 Joint Statistical Meetings in Miami Beach, Florida. The award recognized Dr. Gail's seminal contributions to methods for the assessment of competing risks, surrogate markers, back-calculation estimation of the incidence and prevalence of AIDS, design and analysis of case-control studies, estimation of the number of deaths attributable to obesity and overweight, and estimation of attributable and absolute risk of breast cancer, which Dr. Gail has applied in developing the landmark Breast Cancer Risk Assessment Tool, also known as the Gail Model (<http://www.cancer.gov/bcrisktool/>).

DCEG ANNUAL TOWN MEETING

In June, DCEG held its Annual Town Meeting to celebrate the accomplishments of Division members during the past year. **Joseph F. Fraumeni, Jr., M.D.**, Division Director, welcomed the staff and introduced the featured speaker, Douglas Lowy, M.D., NCI Deputy Director.

In his presentation, Dr. Lowy described current NCI research priorities. These priorities include maintaining a vigorous investigator-initiated research portfolio, expanding research in cancer genomics, and restructuring the clinical trials process. He also gave an update on new NCI appointments and budget issues.

Shelia Hoar Zahm, Sc.D., DCEG Deputy Director, provided a “year in review” of the Division’s research, honors and awards received by DCEG investigators, staff additions and departures, training activities, and other special events. Significant DCEG scientific publications over the past year included findings from studies on obesity and physical activity, the Vitamin D Pooling Project, cancer susceptibility syndromes, HIV and cancer, and

genome-wide association studies. Dr. Zahm also summarized infrastructure improvements and scientific accomplishments at DCEG-affiliated laboratories, including the SAIC Core Genotyping Facility, the NCI DNA Extraction and Staging Laboratory, biorepositories, and the NCI Hormone Measurement Laboratory.

Dr. Fraumeni honored scientific contributions and outstanding service by DCEG members. Fellowship Achievement Awards honored fellows who excelled during the past year and included stipend increases at the next appointment renewal. Recipients were **Jonathan Hofmann, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB), **Alison Mondul, Ph.D.**, Nutritional Epidemiology Branch (NEB), **Sarah Nyante, Ph.D.**, Hormonal and



Douglas Lowy (Photograph credit: Bill Branson)

Reproductive Epidemiology Branch (HREB), and **Sara Schonfeld, Ph.D.**, Radiation Epidemiology Branch (REB).

Awards were also given for DCEG Outstanding Research Papers of 2010 in recognition of exceptional publications from fellows and staff scientists or clinicians. The Division’s Senior Advisory Group judged the competition based on the papers’ impact, innovation, and clarity of thought and language. Five fellows received awards:

Samsiddhi Bhattacharjee, Ph.D., Biostatistics Branch (BB): “Using principal components of genetic variation for robust and powerful detection of gene-gene interactions in case-control and case-only studies,” *American Journal of Human Genetics*

Michael B. Cook, Ph.D. (HREB): “Cigarette smoking and adenocarcinomas of the esophagus and esophagogastric junction: A pooled analysis from the International BEACON Consortium,” *Journal of the National Cancer Institute*



Douglas Lowy, Steven Simon, and Joseph Fraumeni. (Photograph credit: Bill Branson)



Douglas Lowy, Debra Silverman, and Joseph Fraumeni. (Photograph credit: Bill Branson)

Idan Menashe, Ph.D. (formerly of BB): “Pathway analysis of breast cancer genome-wide association study highlights three pathways and one canonical signaling cascade,” *Cancer Research*

Ju-Hyun Park, Ph.D. (BB): “Estimation of effect size distribution from genome-wide association studies and implications for future discoveries,” *Nature Genetics*

Sara Schonfeld, Ph.D. (REB): “Effect of changing breast cancer incidence rates on the calibration of the Gail model,” *Journal of Clinical Oncology*

The recipient in the staff scientist or clinician category was:

Steven L. Simon, Ph.D. (REB): “Radiation doses and cancer risks in the Marshall Islands associated with exposure to radioactive fallout from Bikini and Enewetak nuclear weapons tests,” *Health Physics*

DCEG Special Appreciation Awards were given to **Denise Brandenburg**, Administrative Resource Center, for her skillful management of the Division’s

budget and the development of a valuable automated system for tracking DCEG expenditures at SAIC-Frederick; **Geoffrey Tobias**, Human Genetics Program, for his outstanding technical support and advice, particularly in his role as executive secretary for several genetics-related oversight committees; and **Tawanda (Tee) Roy** (NEB) and **Rashmi Sinha, Ph.D.**, Deputy Chief of NEB, for their selfless administrative and scientific contributions to NEB during the extended illness of the former NEB Branch Chief.

Neal D. Freedman, Ph.D., M.P.H. (NEB), and **Mary H. Ward, Ph.D.** (OEEB), received DCEG Outstanding Mentor Awards in recognition of their exceptional commitment to the growth and productivity of junior scientists. In the nomination by fellows, Dr. Freedman was described as “an exceptional mentor and admirable role model because of his strong work ethic, generosity, and love of science.” Dr. Ward was praised for her skills as “a thoughtful listener, recognizing fellows’ strengths and individuality and offering suggestions on how to build on those areas.”

A DCEG Exemplary Service Award was given to **Debra T. Silverman, Sc.D.**, Chief of OEEB. Recognized as a world-class epidemiologist, Dr. Silverman’s research focuses on the origins of cancers of the bladder and pancreas as well as on the carcinogenic effects of diesel exhausts. Her recent work on bladder cancer has yielded new etiologic insights, including reasons for the persistently high rates reported in New England. Her work on the effects of diesel exhaust exposure among underground miners promises to have significant public health importance.

A DCEG Exemplary Service Award was also given to Dr. Simon. An expert on assessing historical radiation doses from nuclear weapons fallout, Dr. Simon has provided advice over many years to national and international organizations on the health effects of environmental contamination from nuclear testing. In March 2011, he took service to a new level when he was deployed to Japan to advise the U.S. embassy and consulates on health issues related to radiation exposure following the earthquake, tsunami, and damage to a nuclear power plant at Fukushima Daiichi.

Winners of the DCEG Fellows Award for Research Excellence and the DCEG Intramural Research Awards, which had been announced earlier in the year, also received recognition at the Town Meeting. The event was coordinated by **Alyssa Voss, M.P.H.**, Office of Communications and Special Initiatives. ■

—Victoria A. McCallum, M.P.H.

2011 DCEG SUMMER FELLOWS RECOGNITION AND POSTER EVENT

Every year, DCEG welcomes a group of summer fellows, ranging from high school to doctoral students, who conduct various research projects under the mentorship of DCEG scientists. In August, at the 13th Annual DCEG Summer Fellows Recognition and Poster Event, the Division celebrated the accomplishments of 27 talented summer fellows and their 37 DCEG mentors. The event brought together many DCEG staff members, who viewed the posters and discussed the students' projects.

As the featured speakers, **Joseph F. Fraumeni, Jr., M.D.**, DCEG Director, **Shelia Hoar Zahm, Sc.D.**, DCEG Deputy Director, and **Jackie Lavigne, Ph.D., M.P.H.**, Chief of DCEG's Office of Education (OE), shared their insights about developments in cancer epidemiology research and careers in science. Dr. Fraumeni stated that the summer fellows had arrived at DCEG at a very



Summer fellows with event speakers and Office of the Director staff.

exciting time in cancer research, including the fields of epidemiology, genetics, statistics, and related areas. He pointed to the revolutionary advances in genomics that are providing unparalleled opportunities for cancer research and training across the Division and NCI. **Kristin Kiser, M.H.A., M.S.**, fellowship coordinator in OE, with support from

Tess Lee, OE program assistant, hosted and organized the recognition event.

This year, a new feature of the training experience was the Journal Club for Summer Fellows in Cancer Epidemiology: Etiology, Prevention, and Policy, which was organized by several NCI postdoctoral fellows,

2011 DCEG Summer Fellows Posters and Projects

Melissa Braganza, Washington University
Exploring the relationship between ionizing radiation and the risk of brain/CNS tumors
Mentors: **Cari Meinhold Kitahara, Ph.D.**, and **Preetha Rajaraman, Ph.D.**, both of the Radiation Epidemiology Branch (REB)

Nathan Brand, Colorado College
Functional annotation of genetic variants associated with prostate cancer risk
Mentors: **Ludmila Prokunina-Olsson, Ph.D.**, and **McAnthony D. Tarway**, both of the Laboratory of Translational Genomics (LTG)

Laura Burke, George Washington University
Association between telomere length and risk of melanoma
Mentors: **Paula Hyland, Ph.D., M.P.H.**, and **Xiaohong Rose Yang, Ph.D., M.P.H.**, both of the Genetic Epidemiology Branch (GEB)

Evan Caporaso, University of Maryland
Analysis of life technologies/Ambion RNA-SEQ kit for the personal genome machine
Mentor: **Joseph Boland**, Core Genotyping Facility (CGF)

Joanne Chang, University of Michigan School of Public Health
Investigating human herpesvirus 8 infection among adults in Uganda: A factor analysis approach
Mentors: **Sam M. Mbulaiteye, M.D.**, and **Fatma Shebl, M.D., Ph.D.**, both of the Infections and Immunoepidemiology Branch (IIB)

Carrie Epstein, Wake Forest University
Understanding and visualizing large genomic datasets
Mentor: **Kevin B. Jacobs** (CGF)

Nick Estes, University of South Carolina
Taqman genotyping in the CGF Laboratory
Mentor: **Michelle Manning** (CGF)

Shing Han, University of Maryland
Spatially invariant vector quantization for histological analysis in the BREAST Stamp Project
Mentor: **Gretchen L. Gierach, Ph.D.**, Hormonal and Reproductive Epidemiology Branch (HREB)

Julianna Hsing, Winston Churchill High School
A summer journey: HPV, HLA, and cervical cancer
Mentor: **Mahboobeh Safaiean, Ph.D.** (IIB)

Demetric Jordan, Georgia State University
Determinants of organochlorine pesticides in homes in Seattle, Detroit, Iowa, and Los Angeles
Mentors: **Curt DellaValle, Ph.D., M.P.H.**, and **Mary H. Ward, Ph.D.**, both of the Occupational and Environmental Epidemiology Branch

Catherine Kennedy, University of Maryland
Search for functional elements in the TERT-CLPTM1L GWAS region on chromosome 5p15
Mentors: **Laufey Amundadottir, Ph.D.**, and **Jia Jinping, Ph.D.** (both of LTG)

Michael Kovacs, Washington University
Identification of PRKAR1A as a potential melanoma tumor suppressor functioning through MITF regulation
Mentors: **Kevin Brown, Ph.D.**, and **Mai Xu, Ph.D.** (both of LTG)

Alina Kutsenko, Weill Cornell Medical College
Population-based risks of benign brain tumors among one year cancer survivors
Mentors: **Rochelle E. Curtis, M.A.**, and **Preetha Rajaraman, Ph.D.** (both of REB)

including Brandy Heckman-Stoddard, Ph.D., M.P.H., from the NCI Division of Cancer Prevention; **Shih-Wen (Wenny) Lin, Ph.D., M.P.H.**, Nutritional Epidemiology Branch; **Sarah E. Daugherty Weller, Ph.D., M.P.H.**, Occupational and Environmental Epidemiology Branch; and **Hannah P. Yang, Ph.D., Sc.M.**, Hormonal and Reproductive Epidemiology Branch. Discussion topics were taken from recent news events, including reports on potential environmental cancer hazards, developments in cancer genetics, and other noteworthy research findings that deserve epidemiologic attention. Journal club members learned about key methods and general approaches used in epidemiology as well as how to critically evaluate scientific publications.

The summer program is extremely competitive. This year alone, DCEG received

Reflections from 2011 DCEG Summer Fellows

My summer experience at DCEG gave me the opportunity to grow and develop professionally with exciting research projects and great mentoring while also getting to meet other interns and explore Washington, D.C. —Melissa Braganza

My DCEG internship has been one of the most meaningful experiences of my life. Rarely does a student get to try out the life of an NIH researcher over the summer, working collaboratively with and receiving training from some of the best researchers in the world. —Eunah Lee

I came into the lab very nervous but ended up loving my experience. I learned more about genetics than I ever thought I would and made some very good friends. My mentor was wonderful; he was able to answer every question I had and helped me with my first poster and presentations. —Emily Purcell

DCEG is an amazing environment for budding scientists to develop their true passions. I am forever grateful to my mentors for sharing their enthusiasm, knowledge, and commitment to scientific inquiry. —Stephanie Shao

close to 400 applicants. Students interested in applying for 2012 summer fellowships with DCEG are encouraged to learn more about the Division's research. Starting in mid-November,

students can complete the application at <http://dceg.cancer.gov/fellowships/summerprogram>. ■

—Kristin Kiser, M.H.A., M.S.

Eunah Lee, Richard Montgomery High School
Variation of CT dose indices in past and current CT scanners
Mentors: **Stephanie Lamart, Ph.D.**, and **Choonsik Lee, Ph.D.** (both of REB)

Luyang Liu, Barnard College
Exploration of DNA-protein interactions within the promoter region of the PSCA gene
Mentors: **Ludmila Prokunina-Olsson, Ph.D.**, and **Wei Tang, Ph.D.** (both of LTG)

Wayne Liu, Johns Hopkins University
Molecular and histological predictors of BRAF and RAS positive mutations in advanced-stage papillary thyroid cancer
Mentors: **Alina V. Brenner, M.D., Ph.D.**, **Gila Neta, Ph.D., M.P.P.**, and **Alice J. Sigurdson, Ph.D.** (all of REB)

Diana Ly, University of California, Los Angeles
An international comparison of male breast cancer incidence
Mentor: **Michael B. Cook, Ph.D.** (HREB)

Artem Morgun, Taras Shevchenko National University of Kiev, Ukraine
Development of a Monte Carlo radiation transport code for organ dose calculation in patients undergoing radiography examinations
Mentor: **Choonsik Lee, Ph.D.** (REB)

Elizabeth Mosher, Madeira High School
A review of studies on Monte Carlo simulations of proton therapy beams
Mentors: **Stephanie Lamart, Ph.D.**, and **Choonsik Lee, Ph.D.** (both of REB)

Elaine Nghiem, University of Maryland
Does smoking influence breast cancer risk through mammographic density?
Mentor: **Barbara J. Fuhrman, Ph.D.** (HREB)

Emily Purcell, Lehigh University
All mixed up: The role of CEP57 in aneuploidy
Mentor: **Joseph Kovacs** (LTG)

Alexandra Scott-Johnson, University of Maryland
Exploration of functional mechanisms that link the CCNE1 gene and its genetic variants with risk of bladder cancer
Mentors: **Indu Kohaar, Ph.D.**, and **Ludmila Prokunina-Olsson, Ph.D.** (both of LTG)

Stephanie Shao, Yale School of Public Health
The association of quercetin intake and microRNA expression in EAGLE lung cancer tissue
Mentors: **Tram Kim Lam, Ph.D.**, and **Maria Teresa Landi, M.D., Ph.D.** (both of GEB)

Llewellyn Smith, Walt Whitman High School
Body mass index and lung cancer risk among never, former, and current smokers in the NIH-AARP Diet and Health Study
Mentor: **Gretchen L. Gierach, Ph.D.** (HREB)

Kathleen Tatem, St. Mary's College
Serum immunoglobulin free light chain measurements and familial chronic lymphocytic leukemia
Mentors: **Neil E. Caporaso, M.D.**, Chief of GEB, and **Lynn R. Goldin, Ph.D.**, Deputy Chief of GEB

Yenny Webb-Vargas, Johns Hopkins Bloomberg School of Public Health
Temporal trends in reproductive risk factors and estrogen receptor-defined breast cancer incidence
Mentors: **William F. Anderson, M.D., M.P.H.**, and **Ruth M. Pfeiffer, Ph.D.**, both of the Biostatistics Branch

Jeannette Wong, Washington University
Risk of second cancer related to chemotherapy and radiation treatment in long-term survivors of retinoblastoma
Mentor: **Ruth A. Kleinerman, M.P.H.** (REB)

EXPERT PANEL WORKSHOP ON EARLY-LIFE EVENTS AND CANCER

In May, DCEG and the NCI Division of Cancer Control and Population Sciences (DCCPS) sponsored an Expert Panel Workshop on Early-Life Events and Cancer. The event was organized by Workshop Steering Committee members **Robert N. Hoover, M.D., Sc.D.**, Director of the Epidemiology and Biostatistics Program (EBP); **Martha S. Linet, M.D., M.P.H.**, Chief of the Radiation Epidemiology Branch; Somdat Mahabir, Ph.D., M.P.H., from the DCCPS Epidemiology and Genetics Research Program; Nancy Potischman, Ph.D., from the DCCPS Applied Research Program; and **Rebecca Troisi, Sc.D.** (EBP). The primary aim of the workshop was to stimulate and facilitate epidemiologic and molecular research into early-life influences on cancer development in adulthood.

Robert Croyle, Ph.D., Director of DCCPS, started the day by highlighting the significant public and scientific interest in the role of early-life events in cancer and other chronic diseases. He noted that NCI has experienced an increase in requests for funding in this area of research. Dr. Mahabir then gave an overview of the workshop's objectives, which included reviewing the epidemiologic and experimental evidence for early-life events in the cause of various forms of cancer and identifying ways to overcome the methodological challenges in this area of cancer research.

The workshop included presentations by Dr. Hoover and seven members of the expert panel, including Dr. Kjersti Aagaard-Tillery, Baylor College of Medicine; Lucy Anderson, Ph.D., formerly of the NCI Laboratory of Comparative Carcinogenesis; Dr. Zdenko Herceg, International Agency for Research on Cancer; Dr. Robert Hiatt, University of



Early-Life Events and Cancer Working Group: (front) Rebecca Troisi, Lucy Anderson, Martha Linet, Nancy Potischman, and Daniel Medina; (back) Zdenko Herceg, Somdat Mahabir, Robert Hiatt, Steinar Tretli, Robert Hoover, Dimitrios Trichopoulos, and Kjersti Aagaard-Tillery.

California, San Francisco, Comprehensive Cancer Center; Dr. Daniel Medina, Baylor College of Medicine; Dr. Steinar Tretli, Cancer Registry of Norway; and Dr. Dimitrios Trichopoulos, Harvard School of Public Health. The presentations addressed a wide range of topics, including the usefulness of animal models to study *in utero* exposures, potential biological mechanisms mediating prenatal exposures and cancer risk, and statistical tools and epidemiologic approaches that might elucidate events in the disease process.

In the afternoon, the panel and experts from NCI met to address

methodological challenges, identify data gaps, and make recommendations about scientific opportunities, resource needs, and potential funding initiatives. The group's deliberations included a discussion of the need for epidemiologic, clinical, and animal model studies and, especially, interdisciplinary strategies. A summary of the proceedings will be published in a peer-reviewed journal.

For more information, please go to <http://go.usa.gov/8UZ> (case sensitive). ■

—Rebecca Troisi, Sc.D.

NEW DCEG FELLOWS ORGANIZATION

The DCEG Fellows Committee (DFel) was organized in early 2011 by postdoctoral and predoctoral fellows in conjunction with the DCEG Office of Education (OE) to enhance the intramural training experience within the Division. Serving more than 100 DCEG fellows, the committee aims to foster interaction among fellows within DCEG as well as across NCI and NIH.

Since its inauguration, DFel has worked with OE staff to develop DCEG Internet and intranet information useful for fellows, initiated a DCEG epidemiology fellows editorial board, and developed a survey for fellows' ideas on initiatives to enhance their overall research and training experience.

DFel cochairs **Jacqueline Major, Ph.D.**, Nutritional Epidemiology Branch, and **Britton Trabert, Ph.D.**, Hormonal and Reproductive Epidemiology Branch, welcome suggestions, comments, and questions. DFel meetings are open to all DCEG fellows and are scheduled for the fourth Wednesday of every month.

—Britton Trabert, Ph.D.

U.S.–RUSSIA AGREEMENT CONTINUES RADIATION EFFECTS RESEARCH

In July, U.S. Secretary of State Hillary Clinton and Russian Foreign Minister Sergey Lavrov formally extended the Joint Coordinating Committee for Radiation Effects Research agreement, the legal basis for U.S. and Russian Federation scientists to conduct and coordinate scientific research on the health effects of radiation exposure at former Russian nuclear weapons production sites. These sites include the Mayak nuclear facility in the Southern Urals, which began operation in 1948 and produced plutonium for the former Soviet Union's weapons program. Scientists from DCEG's Radiation Epidemiology Branch (REB) are collaborating with Russian scientists to study individuals exposed as a result of Mayak operations. Workers at that facility were exposed to plutonium and to protracted external radiation at much higher doses than nuclear workers in other countries. Offspring of these workers were potentially exposed *in utero*, and people who resided along the Techa River were exposed to radioactive waste that was discharged into the river.

Using radiation dose information from the U.S. Department of Energy under the Russian Health Studies Program,



U.S. Secretary of State Hillary Clinton and Russian Foreign Minister Sergey Lavrov. (Photograph credit: Courtesy of the U.S. Department of State)

REB investigators and their collaborators have evaluated dose-response relationships for radiation-related cancer in these populations. For workers, strong dose-response relationships have been demonstrated between plutonium exposure and cancers of the lung, liver, and bone (the three major sites of plutonium deposition), while external dose-response relationships have been observed for mortality from solid cancer and leukemia. For the Techa River cohort, dose-response relationships have been noted for solid cancer

and leukemia using both mortality and incidence data.

Analyses based on updated follow-up information and improved dose estimates are in progress. These studies are providing unique information on the risk of cancer from protracted radiation exposure that is important for establishing international recommendations on radiation protection. ■

—Ethel S. Gilbert, Ph.D.,
and Sara Schonfeld, Ph.D.

DCEG COLLABORATOR WEI-CHENG YOU RECOGNIZED

DCEG Director **Joseph F. Fraumeni, Jr., M.D.**, recently recognized Dr. Wei-Cheng You, Director of the Beijing Institute for Cancer Research, for his groundbreaking research into the causes and prevention of gastric cancer. A long-time DCEG collaborator and former visiting scientist in DCEG's Biostatistics Branch, Dr. You has been a leader in genetic and epidemiologic studies into the environmental risk factors associated with gastric cancer and precancerous lesions. In a seminal investigation of a high-risk population in China, he was instrumental in conducting and coordinating a long-term intervention trial that has demonstrated a protective effect of antibiotic treatment for *Helicobacter pylori*, the main causal agent for this cancer, as well as protective effects of certain micronutrients.



Mitchell Gail, Joseph Fraumeni, and Wei-Cheng You.

SCIENTIFIC HIGHLIGHTS

ALL CANCERS

Cancer Incidence Among Pesticide Applicators

To investigate the association of atrazine use with cancer risk, the authors utilized information from the Agricultural Health Study, a prospective cohort that includes 57,310 licensed pesticide applicators. They extended a previous analysis of this association with six additional years of follow-up and more than twice as many cancer cases. Overall, 36,357 (68%) of the pesticide applicators reported using atrazine, among which there were 3,146 cases of cancer. There was no increase among atrazine users in overall cancer risk or at most cancer sites among the higher lifetime use or intensity-weighted lifetime day exposure categories compared with the lowest exposure categories. Based on 29 exposed cases of thyroid cancer, there was a significant risk of this cancer in the second and fourth quartiles of intensity-weighted lifetime days. (Beane Freeman LE, Rusiecki JA, Hoppin JA, et al. Atrazine and cancer incidence among pesticide applicators in the Agricultural Health Study [1994–2007]. *Environ Health Perspect* 2011;119:1253–1259)

ALL-CAUSE MORTALITY

Dietary Fiber Intake

To investigate the relationship of dietary fiber intake with total and cause-specific mortality, the authors examined data from the NIH-AARP Diet and Health Study, a prospective cohort study in which diet was assessed using a food-frequency questionnaire at baseline. A total of 20,126 deaths among men and 11,330 deaths among women were identified during the average nine years of follow-up. Fiber intake was associated with a lowered risk of total death (highest vs. lowest quintile: RR = 0.78 among both men and women). Fiber

intake lowered the risk of death from cardiovascular, infectious, and respiratory diseases by 24% to 56% among men and by 34% to 59% among women. An inverse association between dietary fiber intake and cancer death was observed among men but not women. Fiber from grains, but not other sources, was significantly inversely related to total and cause-specific death among both men and women. (Park Y, Subar AF, Hollenbeck A, Schatzkin A. Dietary fiber intake and mortality in the NIH-AARP Diet and Health Study. *Arch Intern Med* 2011;171:1061–1068)

Waist Circumference, Body Mass Index, and Mortality

The authors evaluated the association of waist circumference (WC) and body mass index (BMI) with mortality using data from the NIH-AARP Diet and Health Study for 225,712 women and men. A total of 20,977 deaths were documented during follow-up from 1996 through 2005. Increased WC consistently predicted risk of death due to any cause as well as major causes of death, independent of BMI. WC was related to a 1.37-fold increased risk of death from any cancer and a 1.82-fold increased risk of death from cardiovascular disease, comparing the highest versus lowest WC categories. WC, but not BMI, showed significant positive associations with deaths from lung cancer and chronic respiratory disease. (Leitzmann MF, Moore SC, Koster A, et al. Waist circumference as compared with body-mass index in predicting mortality from specific causes. *PLoS One* 2011;6:e18582)

ANAL CANCER

HPV Vaccine Efficacy

To assess the efficacy of a bivalent HPV 16/HPV 18 vaccine against anal infection with HPV 16, HPV 18, or both, investigators performed an analysis within a cohort of Costa Rican women,

ages 18–25, who were administered the vaccine as part of a randomized, controlled trial to determine its efficacy against persistent cervical HPV infections. At the final follow-up visit four years after vaccination, women who consented provided an anal specimen for a one-time assessment of vaccine efficacy against anal HPV 16/18 infection. The analyses were based on the full cohort of women who provided a specimen and a restricted cohort of women who were negative for both cervical HPV 16 and HPV 18 DNA and who were HPV 16 and HPV 18 seronegative before enrollment. In the full cohort, vaccine efficacy against prevalent HPV 16/18 infection was lower at the anus (62.0%) than at the cervix (76.4%; *p* for interaction by anatomical site = 0.031). In the restricted cohort, vaccine efficacy against anal HPV 16/18 infection was 83.6%, which was similar to vaccine efficacy against cervical HPV 16/18 infection (87.9%). These results demonstrate that the bivalent vaccine affords strong protection

GLOSSARY

CI	Confidence interval
HPV	Human papillomavirus
HR	Hazard ratio
IL	Interleukin
OR	Odds ratio
PLCO	Prostate, Lung, Colorectal, and Ovarian
RR	Relative risk
SEER	Surveillance, Epidemiology and End Results
SNP	Single nucleotide polymorphism

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

against anal HPV infection, particularly among women more likely to be HPV seronegative at enrollment. (Kreimer AR, González P, Katki HA, et al. Efficacy of a bivalent HPV 16/18 vaccine against anal HPV 16/18 infection among young women: A nested analysis within the Costa Rica Vaccine Trial. *Lancet Oncol* 2011;12:862–870)

BLADDER CANCER

Smoking and Bladder Cancer

The authors evaluated the association between tobacco smoking and bladder cancer among 281,394 men and 186,134 women in the NIH-AARP Diet and Health Study cohort who completed a lifestyle questionnaire. During follow-up, incident bladder cancer occurred among 3,896 men and 627 women (144.0 and 34.5 per 100,000 person-years, respectively). Former smokers (119.8 per 100,000 person-years; HR = 2.22) and current smokers (177.3 per 100,000 person-years; HR = 4.06) had higher risks of bladder cancer than never smokers. Compared with a pooled estimate of U.S. data from cohorts initiated between 1963 and 1987, RRs for smoking in the more recent NIH-AARP Diet and Health Study cohort were significantly higher, suggesting that recent changes in the composition of cigarettes and smoking practices (e.g., greater inhalation) are increasing the risks of bladder and perhaps other smoking-related cancers. (Freedman ND, Silverman DT, Hollenbeck AR, et al. Association between smoking and risk of bladder cancer among men and women. *JAMA* 2011;306:737–745)

BREAST CANCER

Breast Cancer Trends in the United States

To investigate U.S. time trends for the overall incidence of breast cancer and for estrogen receptor positive (ER+) and estrogen receptor negative (ER-) breast cancers, the authors developed a simple imputation method to correct invasive

MAJOR EDITORIALS, COMMENTARIES, AND REVIEWS BY DCEG SCIENTISTS

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Freedman LS, Schatzkin A, et al. Dealing with dietary measurement error in nutritional cohort studies. *J Natl Cancer Inst* 2011;103:1086–1092

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Wentzensen IM, Mirabello L, Pfeiffer RM, Savage SA. The association of telomere length and cancer: A meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2011;20:1238–1250

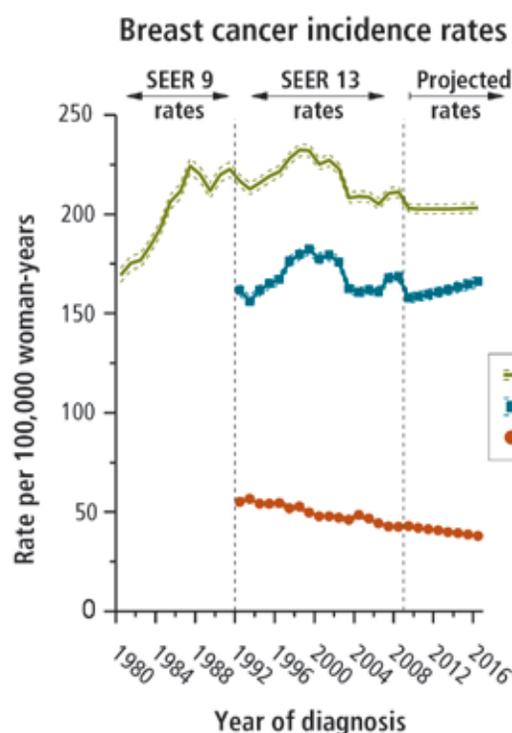


Figure 1. Incidence rates for breast cancer overall and imputed rates of estrogen receptor positive (ER+) and estrogen receptor negative (ER-) breast cancers for early (1980–1991), contemporary (1992–2008), and future (2009–2016) periods. Incidence rates were age standardized to the year 2000 U.S. standard population and expressed per 100,000 woman-years among women aged 30–84 years, and 95% CIs are shown (dashed lines). (Anderson WF, et al. *J Natl Cancer Inst* 2011)

female breast cancer incidence for missing or unknown ER expression using data from the NCI SEER Program during 1980–2008. Corrected rates of ER+ and ER- breast cancers were used to calculate age-standardized incidence rates, estimated annual percent changes, and projections derived from age-period-cohort models. The incidence of breast cancer overall stabilized to near 200 per 100,000 woman-years by 2007–2008, reflecting a transient decrease in ER+ cancers and a steady decrease of ER- cancers (see Figure 1). The projected incidence rate for breast cancer overall through the year 2016 was similar to the incidence rate during 2007–2008. Rates of ER+ cancers were projected to increase 5.3% and rates of ER- breast cancers were projected to decrease 11.4% during 2009–2016. (Anderson WF, Katki HA, Rosenberg PS. Incidence of breast cancer in the United States: Current and future trends. *J Natl Cancer Inst* 2011;103:1397–1402)

Risk Factor Modification and Breast Cancer Risk

The authors developed a model to predict the absolute risk of breast cancer that included five nonmodifiable and three modifiable risk factors, using data from a case-control study of women in Italy (2,569 cases and 2,588 controls) and incidence and mortality data from the Florence Registries. The model was reasonably well calibrated (ratio of expected to observed cancers = 1.10, CI = 0.96–1.26), but the discriminatory accuracy was modest. The absolute risk reduction from exposure modifications was nearly proportional to the risk before the risk factors were modified and increased with age and risk projection time span. Mean 20-year reductions in absolute risk among women aged 65 years were 1.6% in the entire population, 3.2% among women with a positive family history of breast cancer, and 4.1% among women

who accounted for the highest 10% of the total population risk. (Petraconi E, Decarli A, Schairer C, et al. Risk factor modification and projections of absolute breast cancer risk. *J Natl Cancer Inst* 2011;103:1037–1048)

CERVICAL CANCER

Vaccine Prevention Trial

The authors evaluated the efficacy of an HPV 16/18 vaccine against one-year persistent infection, stratified by age and sexual behavior in the Costa Rica Vaccine Trial, a community-based, randomized trial of 7,466 healthy women. According-to-protocol (ATP) cohorts included compliant HPV-negative women; intention-to-treat (ITT) included all randomized women. ATP vaccine efficacy was 90.9% against HPV 16/18 infection, 44.5% against HPV 31/33/45 infection, and 12.4% (CI = –3.2–25.6) against any oncogenic infection. Overall ITT vaccine efficacy against HPV 16/18 was 49.0%, but ATP and ITT vaccine efficacy reached almost 100% in year four of the follow-up. ATP efficacy against HPV 16/18 was similar by age, but ITT efficacy was highest among youngest women (68.9% among 18- to 19-year-olds; 21.8% among 24- to 25-year-olds) and 79.8% among virgins. Among previously unexposed women, vaccination was highly effective against HPV 16/18 and showed partial cross-protection against HPV 31/33/45. The benefit was maximal when vaccination was given to young women before initiation of sexual activity. (Herrero R, Wacholder S, Rodriguez AC, et al. Prevention of persistent human papillomavirus [HPV] infection by a HPV 16/18 vaccine: A community-based randomized clinical trial in Guanacaste, Costa Rica. *Cancer Discov* 2011; [E-pub ahead of print])

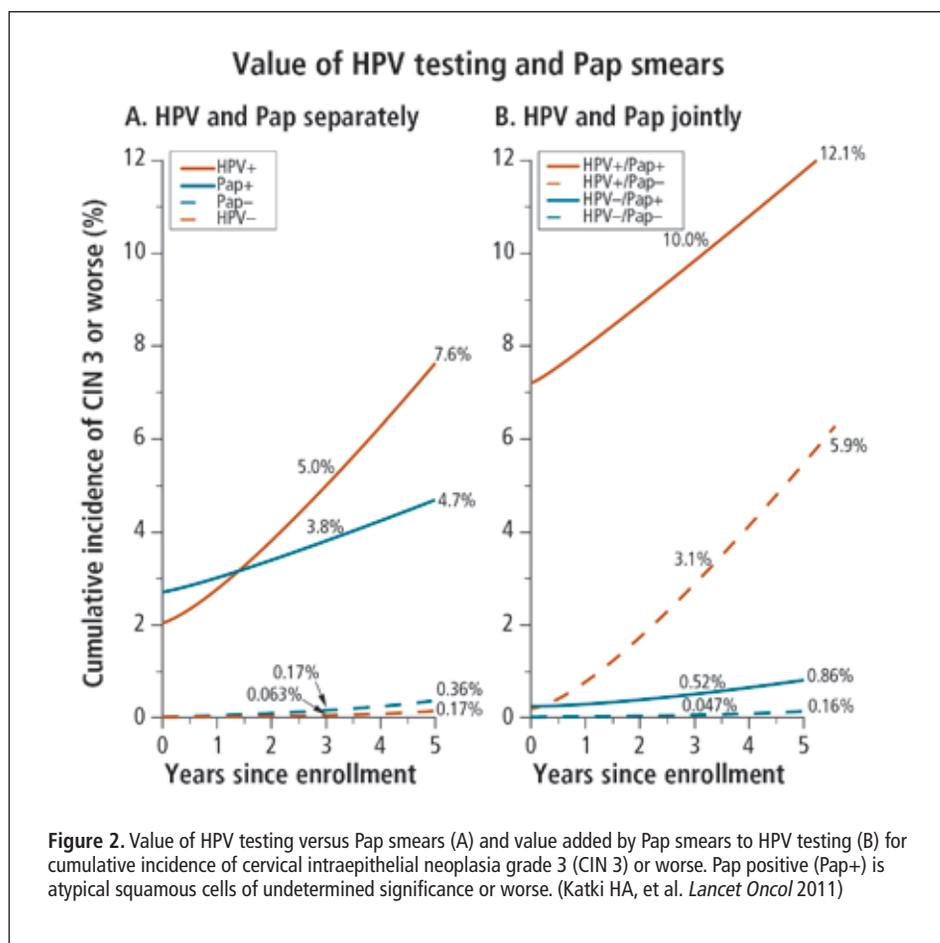
Number of Vaccine Doses

The authors evaluated the vaccine efficacy of fewer than three doses of an HPV 16/18 vaccine using data from the Costa Rica Vaccine Trial. Women were randomly assigned to receive three doses

of the HPV 16/18 vaccine or a control vaccine and were followed for incident HPV 16 or HPV 18 infection that persisted in visits that were 10 or more months apart (median follow-up = 4.2 years). A total of 5,967 women received three vaccine doses (2,957 HPV, 3,010 control), 802 received two doses (422 HPV, 380 control), and 384 received one dose (196 HPV, 188 control). Incident HPV 16 or HPV 18 infections that persisted for one year were unrelated to dosage of the control vaccine. Vaccine efficacy was 80.9% for three doses of the HPV vaccine (CI = 71.1%–87.7%; 25 and 133 events in the HPV and control arms, respectively), 84.1% for two doses (CI = 50.2%–96.3%; 3 and 17 events), and 100% for one dose (CI = 66.5%–100%; 0 and 10 events). Four years after vaccination of women who appeared to be uninfected, this nonrandomized analysis suggests that two doses of the HPV 16/18 vaccine, and maybe even one dose, are as protective as three doses. (Kreimer AR, Rodriguez AC, Hildesheim A, et al. Proof-of-principle evaluation of the efficacy of fewer than three doses of a bivalent HPV16/18 vaccine. *J Natl Cancer Inst* 2011;103:1444–1451)

Concurrent Testing for HPV and Cervical Cytology

The authors assessed the five-year cumulative incidence, starting in 2003–2005, of cervical cancer and cervical intraepithelial neoplasia grade 3 (CIN 3) or worse among 331,818 women aged 30 years and older who enrolled in HPV/cervical cytology co-testing at Kaiser Permanente Northern California. Among 315,061 women negative by HPV testing, the five-year cumulative incidence of cancer was 3.8 per 100,000 women per year, which was slightly higher than that for the 306,969 women who were negative by both HPV and cervical cytology (3.2 per 100,000) and half the cancer risk of the 319,177 women who were negative by cervical cytology (7.5 per 100,000) (see Figure 2). Abnormal cytology



greatly increased cumulative incidence of CIN 3 or worse over five years for the 16,757 women positive by HPV testing. Although statistically significant, abnormal cytology did not increase the five-year risk of CIN 3 or worse for women negative by HPV testing to a substantial level. The results indicate that for women aged 30 years and older in routine clinical practice who are negative by co-testing, three-year screening intervals in routine clinical practice are adequate because a single negative test for HPV is sufficient to assure against cervical cancer over five years. (Katki HA, Kinney WK, Fetterman B, et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: A population-based study in routine clinical practice. *Lancet Oncol* 2011;12:663–672)

COLORECTAL CANCER

Iron Homeostasis and Colorectal Adenoma

The authors conducted a case-control study within the PLCO Cancer Screening Trial to evaluate prospectively assessed dietary intake and serum measures of iron in relation to colorectal adenoma risk among 356 cases of colorectal adenoma and 396 polyp-free controls. Variation in eight genes involved in iron homeostasis was investigated among an additional 1,126 cases and 1,173 controls. A positive association was observed between red meat intake and colorectal adenoma (quartile 4 vs. quartile 1: OR = 1.59). Risk was inversely associated with serum total iron binding capacity and unsaturated iron binding capacity (quartile 4 vs. quartile 1: OR = 0.57 and OR = 0.62, respectively). However, there was no

association with serum ferritin, iron, or transferrin saturation or with polymorphisms in genes involved in iron homeostasis. (Cross AJ, Sinha R, Wood RJ, et al. Iron homeostasis and distal colorectal adenoma risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Cancer Prev Res [Phila]* 2011;4:1465–1475)

FAMILIAL CANCER

Confirmation of Family Cancer History

In the population-based Connecticut Family Health Study, participants reported cancer in 20,578 first-degree relatives (FDR) and second-degree relatives (SDR). Of those, 2,605 relatives were sampled for confirmation of reports on breast, colorectal, prostate, and lung cancer from state cancer registries, Medicare databases, the National Death Index, death certificates, and health care facility records. Sensitivity and positive predictive value were low to moderate and varied by cancer type: 60.2% and 40.0%, respectively, for lung cancer; 27.3% and 53.5% for colorectal cancer; 61.1% and 61.3% for breast cancer; and 32.0% and 53.4% for prostate cancer. Specificity and negative predictive value were higher than 95% for all four cancer types. Cancer history reports for FDR were more accurate than reports for SDR. Efforts to improve accuracy are needed in settings where family history is collected to ensure appropriate risk assessment and clinical care recommendations. (Mai PL, Garceau AO, Graubard BI, et al. Confirmation of family cancer history reported in a population-based survey. *J Natl Cancer Inst* 2011;103:788–797)

GASTRIC CANCER

Serum Ghrelin Concentration

The authors evaluated serum levels of the hormone ghrelin among 261 gastric noncardia adenocarcinoma (GNCA) patients, 98 esophagogastric junctional adenocarcinoma (EGJA) patients, and

441 control subjects in the prospective Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Risks of both GNCA and EGJA were increased for individuals in the lowest quartile of serum ghrelin compared with those in the highest quartile (GNCA: OR = 5.63; EGJA: OR = 4.90). These results suggest a potential role for gastric hormones in carcinogenesis. (Murphy G, Kamangar F, Dawsey SM, et al. The relationship between serum ghrelin and the risk of gastric and esophagogastric junctional adenocarcinomas. *J Natl Cancer Inst* 2011;103:1123–1129)

LIVER CANCER

Metabolic Syndrome and Liver Cancer

The authors evaluated the prevalence of metabolic syndrome and other risk factors for hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) among 3,649 HCC and 743 ICC cases diagnosed between 1993 and 2005 in the SEER-Medicare database and among a 5% sample of individuals (195,953 persons) residing in the same SEER regions as the case subjects. Metabolic syndrome was significantly more common among persons who developed HCC (37.1%) or ICC (29.7%) than among the comparison group (17.1%). In adjusted multiple logistic regression analyses, metabolic syndrome remained significantly associated with increased risk of HCC (OR = 2.13) and ICC (OR = 1.56). (Welzel TM, Graubard BI, Zeuzem S, et al. Metabolic syndrome increases the risk of primary liver cancer in the United States: A study in the SEER-Medicare database. *Hepatology* 2011;54:463–471)

LUNG CANCER

Circulating Cytokines and Lung Cancer

The authors analyzed circulating cytokines as inflammation biomarkers among 270 lung cancer cases and 296 controls in the NCI-Maryland

case-control study. Results were validated among 532 cases and 595 controls in the prospective PLCO Cancer Screening Trial. Serum IL-6 and IL-8 levels were associated with lung cancer risk in both the NCI-Maryland study (IL-6: OR = 3.29; IL-8: OR = 2.06) and the PLCO study (IL-6: OR = 1.48, CI = 1.04–2.10; IL-8: OR = 1.57), comparing the highest to the lowest quartiles. In the PLCO study, increased IL-6 levels were associated only with lung cancer diagnosed within two years of blood collection, whereas increased IL-8 levels were associated with cancer diagnosed more than two years after blood collection. The 10-year standardized absolute risk (AR) of lung cancer in the PLCO study was highest among current smokers with high IL-8 and C-reactive protein levels (AR = 8.01%). (Pine SR, Mechanic LE, Enewold L, et al. Increased levels of circulating interleukin 6, interleukin 8, C-reactive protein, and risk of lung cancer. *J Natl Cancer Inst* 2011;103:1112–1122)

LYMPHOMA

Immune Markers and Non-Hodgkin Lymphoma

In a nested case control study within the PLCO Cancer Screening Trial, selected cytokines (IL-4, IL-6, IL-10, and TNF- α) and other immune markers (soluble TNF receptor 1 [sTNF-R1], sTNF-R2, C-reactive protein, and sCD27) were measured in prediagnostic serum specimens from 297 incident non-Hodgkin lymphoma (NHL) cases and 297 controls. NHL risk was significantly associated with elevated serum levels of sTNF-R1 (quartile 4 vs. quartile 1: OR = 1.7) and sCD27 (OR = 5.3). These associations persisted in analyses based on cases diagnosed longer than six years following blood collection. Elevated levels of IL-10, TNF- α , and sTNF-R2 were also significantly associated with increased risk of NHL; however, these associations weakened with increasing time from blood collection to

case diagnosis and were null for cases diagnosed more than six years after collection. The findings support a role for subclinical inflammation and chronic B-cell stimulation in lymphomagenesis. (Purdue MP, Lan Q, Bagni R, et al. Prediagnostic serum levels of cytokines and other immune markers and risk of non-Hodgkin lymphoma. *Cancer Res* 2011;71:4898–4907)

OSTEOSARCOMA

Genetic Variation Associated with Osteosarcoma

To understand the contribution of genes involved in DNA repair, ribosomal function, growth/hormone, and bone formation to osteosarcoma (OS) pathogenesis, the authors evaluated 4,836 tag-SNPs across 255 candidate genes among 96 OS cases and 1,426 controls. Twelve SNPs in growth or DNA repair genes were significantly associated with OS, including four SNPs in the DNA repair gene *FANCM* and two SNPs downstream of the growth hormone gene *GHI*. One SNP in the region of each of the following genes was significant: *MDM2*, *MPG*, *FGF2*, *FGFR3*, *GNRH2*, and *IGF1*. The results indicate that several SNPs in biologically plausible pathways are associated with the risk of OS. (Mirabello L, Yu K, Berndt SI, et al. A comprehensive candidate gene approach identifies genetic variation associated with osteosarcoma. *BMC Cancer* 2011;11:209)

PANCREATIC CANCER

Advanced Glycation End Products and Pancreatic Cancer Etiology

The authors examined prediagnostic measures of N^ε-(carboxymethyl)-lysine (CML)-advanced glycation end products (AGEs) and soluble receptors for AGEs (sRAGE) with pancreatic cancer in 29,133 Finnish male smokers within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. CML-AGE, sRAGE, glucose, and insulin concentrations were measured in fasting serum

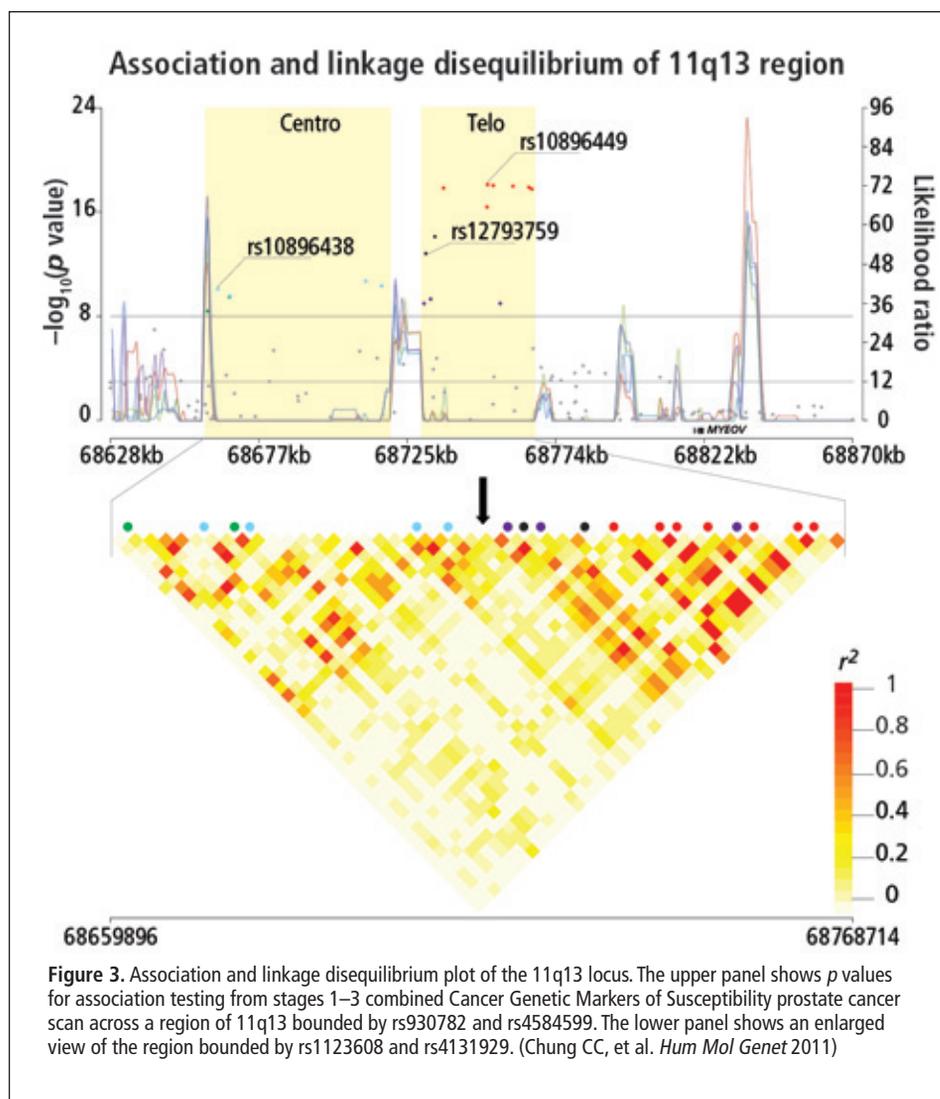


Figure 3. Association and linkage disequilibrium plot of the 11q13 locus. The upper panel shows p values for association testing from stages 1–3 combined Cancer Genetic Markers of Susceptibility prostate cancer scan across a region of 11q13 bounded by rs930782 and rs4584599. The lower panel shows an enlarged view of the region bounded by rs1123608 and rs4131929. (Chung CC, et al. *Hum Mol Genet* 2011)

from 255 incident pancreatic cancer cases and from 485 randomly sampled subcohort participants. CML-AGE levels were not associated with pancreatic cancer (fifth quintile vs. first quintile: RR = 0.68, CI = 0.38–1.22). In contrast, sRAGE levels were inversely associated with pancreatic cancer (fifth quintile vs. first quintile: RR = 0.46, CI = 0.23–0.73). Further adjustment for glucose or insulin levels did not change the observed associations. (Jiao L, Weinstein SJ, Albanes D, et al. Evidence that serum levels of the soluble receptor for advanced glycation end products are inversely associated with pancreatic cancer risk: A prospective study. *Cancer Res* 2011;71:3582–3589)

PROSTATE CANCER

Fine Mapping Chromosome 11q13

Genome-wide association studies have identified prostate cancer susceptibility alleles on chromosome 11q13. As a part of the Cancer Genetic Markers of Susceptibility initiative, the authors fine mapped the region flanking the most significant marker, rs10896449, among 10,272 prostate cancer cases and 9,123 controls using 120 common SNPs selected by a two-staged tagging strategy. Single-locus analysis identified 18 SNPs below genome-wide significance, with rs10896449 being the most significant ($p = 7.97 \times 10^{-19}$). Multi-locus models identified a second association at rs12793759 (OR = 1.14, $p = 4.76 \times 10^{-5}$)

that was independent of rs10896449. A third detected association, rs10896438, was independent of both rs10896449 and rs12793759 (OR = 1.07, $p = 5.92 \times 10^{-3}$). The observation of a recombination hotspot that separates rs10896438 from rs10896449 and rs12793759 as well as low linkage disequilibrium corroborates the finding of three independent signals (see Figure 3 on page 23). (Chung CC, Ciampa J, Yeager M, et al. Fine mapping of a region of chromosome 11q13 reveals multiple independent loci associated with risk of prostate cancer. *Hum Mol Genet* 2011;20:2869–2878)

Fine Mapping Chromosome 19q13.33

Germline variants in the gene that encodes the prostate-specific antigen (PSA) protein (KLK3) have been associated with serum PSA levels and prostate cancer. The authors fine mapped the KLK3 locus by genotyping tag SNPs among 3,522 prostate cancer cases and 3,338 controls from five case-control studies. The authors did not observe a strong association between the KLK3 variant and prostate cancer risk, but three highly correlated SNPs (rs17632542, rs62113212, and rs62113214) were associated with prostate cancer (OR = 0.77, CI = 0.67–0.89, $p = 3.41 \times 10^{-4}$). The signal was apparent only for nonaggressive prostate cancer cases with Gleason score < 7 and disease stage < III. Baseline PSA levels were 43.7% higher in controls with no minor alleles than in controls with one or more minor alleles at any one of the three SNPs. The results suggest that germline KLK3 variants may influence the diagnosis of nonaggressive prostate cancer by influencing serum PSA levels and subsequent likelihood of biopsy. (Parikh H, Wang Z, Pettigrew KA, et al. Fine mapping the KLK3 locus on chromosome 19q13.33 associated with prostate cancer susceptibility and PSA levels. *Hum Genet* 2011;129:675–685)

Gene-Gene Interactions and Prostate Cancer

The authors used data from the Cancer Genetic Markers of Susceptibility program to explore possible interactions between known prostate cancer susceptibility loci and SNPs. Stage I included 523,841 SNPs in 1,175 cases and 1,100 controls. Stage II included 27,383 SNPs in an additional 3,941 cases and 3,964 controls. Several noteworthy interacting SNP pairs were identified through empirical Bayes analysis, although none reached genome-wide significance. An interaction was found between the major prostate cancer susceptibility locus in the subregion of 8q24 that contains *POU5F1B* and an intronic SNP in the transcription factor *EPAS1*, which has potentially important functional implications for 8q24. Another noteworthy result involved interaction of a known prostate cancer susceptibility marker near the prostate protease genes *KLK2* and *KLK3* with an intronic SNP in *PRXX2*. (Ciampa J, Yeager M, Amundadottir L, et al. Large-scale exploration of gene-gene interactions in prostate cancer using a multistage genome-wide association study. *Cancer Res* 2011;71:3287–3295)

Serum Retinol and Prostate Cancer

The authors used high-performance liquid chromatography to measure serum retinol levels from men in the prospective Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study cohort at baseline ($n = 29,104$) and after three years ($n = 22,843$). Men with higher retinol concentrations at baseline were more likely to develop prostate cancer (quintile 5 vs. quintile 1: HR = 1.19), and results were similar for aggressive disease. Men who were in the highest quintile for retinol levels at baseline and after three years had the greatest increased risk (HR = 1.31). (Mondul AM, Watters JL, Männistö S, et al. Serum retinol and risk of prostate cancer. *Am J Epidemiol* 2011;173:813–821)

TESTICULAR CANCER

Adult Height and Testicular Cancer

The authors genotyped 15 height-related SNPs among 561 cases and 676 controls in the U.S. Servicemen's Testicular Tumor Environmental and Endocrine Determinants case-control study. Two SNPs were found to be associated with risk of testicular germ cell tumors (TGCT): rs6060373 (CC vs. TT: OR = 1.51) and rs143384 (CC vs. TT: OR = 1.53). No individual SNP attenuated the association between height and TGCT. (Cook MB, Chia VM, Berndt SI, et al. Genetic contributions to the association between adult height and testicular germ cell tumors. *Int J Epidemiol* 2011;40:731–739)

THYROID CANCER

Dietary Nitrate and Nitrite

To assess whether dietary nitrate and nitrite are associated with thyroid cancer risk overall and by subtype, the investigators used data from the NIH-AARP Diet and Health Study, a prospective cohort of 490,194 men and women ages 50–71 years in 1995–1996. Dietary intakes were assessed using a food frequency questionnaire. After an average of seven years of follow-up, 370 incident thyroid cancer cases with complete dietary information were identified. Among men, increasing nitrate intake was positively associated with thyroid cancer risk (highest vs. lowest quintile: RR = 2.28); however, no trend was observed among women. Nitrite intake was not associated with overall risk of thyroid cancer among either men or women. Positive associations were found between nitrate intake and both papillary (RR = 2.10) and follicular thyroid cancer (RR = 3.42) among men, while nitrite intake was positively associated with follicular thyroid cancer (RR = 2.74) among men. These results support a role of nitrate in thyroid cancer risk. (Kilfoy BA, Zhang Y, Park Y, et al. Dietary nitrate and nitrite and the risk of thyroid cancer in the NIH-AARP Diet and Health Study. *Int J Cancer* 2011;129:160–172)

DCEG PEOPLE IN THE NEWS

In June, **Christian C. Abnet, Ph.D., M.P.H.**, and **Sanford M. Dawsey, M.D.**, both of the Nutritional Epidemiology Branch (NEB), gave talks at the Golestan University of Medical Sciences and the Ardabil University of Medical Sciences in Iran. Dr. Abnet spoke on “The role of genome-wide association studies in uncovering the etiology of upper gastrointestinal cancers.” Dr. Dawsey spoke on “Early detection of esophageal squamous cell carcinoma” and “Polycyclic aromatic hydrocarbon exposure—A universal risk factor for esophageal squamous cell carcinoma?”

In July, **Amy Berrington de González, D.Phil.**, Radiation Epidemiology Branch (REB), spoke on “Diagnostic radiation exposure and cancer—Updated attributable risk estimates” at the International Agency for Research on Cancer in Lyon, France. Also in July, she gave a talk on “Estimated cancer risks from diagnostic medical radiation exposures” at the Symposium on Medical Diagnostic Radiation Exposure and Cancer Risk 2011 at the Netherlands Cancer Institute in Amsterdam.

In August, **Aaron E. Blair, Ph.D., M.P.H.**, a scientist emeritus in the Occupational and Environmental Epidemiology Branch (OEEB), was appointed to the Ontario Independent Fact-Finding Panel on Herbicide 2,4,5-T. The purpose of the panel is to evaluate the use of this herbicide in Ontario, Canada, over the past several decades and to consider possible health effects from human exposure.

In May, **Stephen J. Chanock, M.D.**, Chief of the Laboratory of Translational Genomics (LTG) and Director of the NCI Core Genotyping Facility, presented a talk on “The heritable component of cancer: Insights from genome-wide association studies (GWAS) and the steps beyond” at the Hefei 2011 GWAS workshop, which was sponsored by *Nature Genetics* and the Anhui Medical University in China.

In May, several DCEG investigators gave invited talks at the European Research Organisation on Genital Infection and Neoplasia (EUROGIN) 2011 meeting in Lisbon, Portugal. **Anil K. Chaturvedi, Ph.D.**, Infections and

Immunoepidemiology Branch (IIB), spoke on the epidemiology of human papillomavirus (HPV)-associated head and neck cancers; **Aimée R. Kreimer, Ph.D.** (IIB), discussed HPV vaccination efficacy with less than three doses as well as oral HPV infection; and **Nicolas Wentzensen, M.D., Ph.D.**, Hormonal and Reproductive Epidemiology Branch (HREB), spoke on several topics, including HPV natural history, HPV dysplasia and anal cancer following HPV infection, and HPV genotyping.

In June, **Cher Dallal, Ph.D.**, and **Gretchen L. Gierach, Ph.D.**, both of HREB, received a Supplemental Funding Award to Advance Research on Cancers in Women from the NCI Office of Science Planning and Assessment and the NIH Office of Research on Women's Health for a research proposal titled “Urinary estrogens and estrogen metabolites in relation to objective measures of physical activity among controls in the NCI Polish Breast Cancer Study.” **Mark E. Sherman, M.D.** (HREB), received a Conference Supplement Award for his proposal to hold a workshop on “Postpartum breast remodeling, lactation and breast cancer risk: Towards improved assessment and prevention.” **Bu-Tian Ji, M.D., Dr.P.H.** (OEEB), received a Conference Supplement Award for his proposal titled “Opportunities and changes in cancer research among women in developing countries.”

In June, **Eric A. Engels, M.D., M.P.H.** (IIB), gave an invited talk on “Cancer risk in U.S. transplant recipients” at the University of Alberta in Edmonton, Canada.

In June, **Mitchell H. Gail, M.D., Ph.D.**, Biostatistics Branch, gave an invited talk on “Some problems arising in the

JONATHAN SAMET GIVES NIH GORDON LECTURE

In May, Dr. Jonathan Samet, a professor and the Flora L. Thornton Chair of the Department of Preventive Medicine at the Keck School of Medicine and Director of the Institute for Global Health at the University of Southern California, presented the annual NIH Robert S. Gordon, Jr., Lecture in Epidemiology. A former member of the NCI Board of Scientific Counselors, Dr. Samet was recently appointed to the National Cancer Advisory Board.

His lecture, “Big epidemiology for big problems,” focused on characterizing the role of epidemiologic evidence in scientific problem solving and on creating systems-based approaches that inform medical and public health practice.

This lecture series was established in 1995 as a tribute to Dr. Gordon for his distinguished service in coordinating prevention-related research and clinical trials across NIH. To view Dr. Samet's lecture, go to <http://go.usa.gov/8UB> (case-sensitive).

development and evaluation of models of absolute risk” at a meeting of the International Chinese Statistical Association in New York, New York.

In June, **Gretchen L. Gierach, Ph.D.** (HREB), spoke on “Localized volumetric mammographic density: A novel approach for understanding the molecular epidemiology of breast cancer” at the Fifth International Workshop on Breast Densitometry and Breast Cancer Risk Assessment in San Francisco, California.

In June, **James J. Goedert, M.D.** (IIB), gave an invited talk on “The human microbiota: Striving for health with 100,000,000,000,000 of our closest collaborators” at the Kaiser Permanente Colorado Institute for Health Research in Denver.

In September, **Maureen C. Hatch, Ph.D.** (REB), cochaired a symposium with Dr. Elisabeth Cardis of the Centre for Research in Environmental Epidemiology titled “Lessons learned 25 years post-Chernobyl: Health effects of early life and later exposures” at the 2011 Congress of the International Society

for Environmental Epidemiology in Barcelona, Spain. At the symposium, Dr. Hatch presented a paper on “*In utero* exposure to Chernobyl fallout in Ukraine and subsequent risk of thyroid and non-thyroid cancers.” In connection with the 25th anniversary of the Chernobyl nuclear accident, Dr. Hatch delivered a number of presentations. She spoke at the National Academy of Medical Sciences in Kiev, Ukraine, in March; at the United Nations Headquarters in New York, New York, in April; and at both the University of Toronto in Canada (via webinar) and the Chernobyl Challenge Briefing with the U.S. Congress in Washington, D.C., in May.

Ann W. Hsing, Ph.D. (IIB), gave invited talks on “Promises and challenges of conducting epidemiologic studies in Africa” at the July NCI Cancer Health Disparities Program Meetings 2011 in Bethesda, Maryland, and on “Epidemiology of gallbladder cancer: Implication of female excess” at the Frontiers in Global Health Symposium in June in Shanghai, China.

In July, **Christian Kratz, M.D.**, Clinical Genetics Branch (CGB), presented a poster on “Overlap between cancer and developmental syndrome genes” at the NCI Translational Science Meeting 2011 in Washington, D.C. At the same meeting, **Nicolas Wentzensen, M.D., Ph.D.** (HREB), presented a poster on “A framework to discover methylation markers for etiologic heterogeneity and early detection of endometrial cancers.”

In June, **Aimée R. Kreimer, Ph.D.** (IIB), was invited to present to the Advisory Committee on Immunization Practices at the Centers for Disease Control and Prevention on HPV-associated oropharyngeal cancer. Dr. Kreimer provided background to inform the continued decision-making process as to whether the HPV vaccine recommendation should be extended beyond females to include males.

Shih-Wen (Wenny) Lin, Ph.D., M.P.H. (NEB), received the 2011 Cancer Prevention Research Training Merit Award from the NCI Cancer Prevention Fellowship Program. The award places her in the top 10 percent of Cancer

DCEG FELLOWS PRESENT AT THE 2011 NIH SPRING RESEARCH FESTIVAL

In May, six DCEG postbaccalaureate fellows presented posters as part of the 2011 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 more than 300 postbaccalaureate fellows as well as fellows in the Clinical Research Training Program and the Howard Hughes Medical Institute-NIH Research Scholars Program.

Dianna Buckett, working jointly with the Infections and Immunoepidemiology Branch (IIB) and the Laboratory of Translational Genomics (LTG), and **McAnthony D. Tarway** (LTG), received awards for outstanding posters at the event.

The following DCEG posters were displayed at the festival:

Meta-analysis of IL28B rs12979860 genotype and clearance of hepatitis C virus
Dianna Buckett (IIB and LTG)
Mentor: **Thomas R. O’Brien, M.D., M.P.H.** (IIB)

Relationship between stomach dimension and body mass index based on patient computed tomography image analysis
Rebecca Imran, Radiation Epidemiology Branch (REB)
Mentor: **Choonsik Lee, Ph.D.** (REB)

Post-GWAS functional characterization of pancreatic cancer susceptibility loci on chromosome 13
Jane Kim (LTG)
Mentor: **Laufey Amundadottir, Ph.D.** (LTG)

Circulating insulin and risk of melanoma in Finnish men

Christine Kiruthu (IIB)
Mentors: **Demetrius Albanes, M.D.**, and **Jacqueline Major, Ph.D.** (both of the Nutritional Epidemiology Branch)

Association of breast cancer risk factors with characteristics of terminal ductal lobular units in breast tissue

Laura Linville, Hormonal and Reproductive Epidemiology Branch (HREB)
Mentors: **Gretchen L. Gierach, Ph.D.**, and **Jonine D. Figueroa, Ph.D., M.P.H.** (both of HREB)

Genetic variants within JAZF1 are associated with differential binding of androgen receptor, altered mRNA expression and risk of prostate cancer
McAnthony D. Tarway (LTG)
Mentor: **Ludmila Prokunina-Olsson, Ph.D.** (LTG)

Prevention Fellows and recognizes the outstanding progress she has made during her fellowship.

In May, **Yikyung Park, Sc.D.** (NEB), gave a talk titled “Biomarker-based validation of diet and physical activity assessment in the NIH-AARP Diet and Health Study” at the Korea Centers for Disease Control and Prevention in Osong, Korea.

In May, **Alexander Pemov, M.D., Ph.D.** (CGB), received a Merit Award from the NCI Center for Cancer Research’s Pediatric Oncology Branch for his winning poster at the Branch’s annual “Research Round-up.” His poster, “Extensive whole-chromosome aberrations detected by SNP array in a neurofibromatosis type 1-associated glomus tumor,” won the category for research nurses, biologists, chemists, and lab technicians.

In June, **Vikrant Sahasrabudhe, M.B.B.S., Dr.P.H.** (HREB), gave an invited talk on “HPV and cervical cancer: Overview of epidemiology and prevention” at the Annual Meeting of the Adult AIDS Clinical Trials Group Network in Washington, D.C. Dr. Sahasrabudhe also received a grant award through the Intramural-to-India initiative funded by the NIH Office of AIDS Research. This joint initiative seeks to develop and expand crucial research infrastructure and capacity building between U.S. and Indian biomedical research communities. In collaboration with **Nicolas Wentzensen, M.D., Ph.D.** (HREB), and Dr. Philip E. Castle (formerly of HREB), Dr. Sahasrabudhe will conduct a study among HIV-infected women to evaluate two novel, lower-cost, and potentially sustainable HPV-based biomarkers for improving secondary prevention of cervical cancer.

In May, **Mark E. Sherman, M.D.** (HREB), presented the Paul Kneafsey Memorial Lecture, “Endometrial carcinogenesis: From progression to prevention,” at the University of Calgary in Alberta, Canada, where he also served as chief adjudicator for Pathology Research Day. In June, Dr. Sherman gave an NCI Center of Excellence in Integrative Cancer Biology and Genomics lecture titled “From etiology to molecular pathology of cancer: Opportunity for intramural collaborations” in Bethesda, Maryland.

In June, **Meredith Shiels, Ph.D.** (IIB), presented at the NCI HIV and AIDS Malignancy Branch Seminar on “Impact of the AIDS epidemic on the U.S. burden of Kaposi sarcoma, non-Hodgkin lymphoma and cervical cancer.”

In February, **McAnthony Tarway** (LTG), a postbaccalaureate fellow mentored by **Ludmila Prokunina-Olsson, Ph.D.** (LTG), won a travel award for an Outstanding Oral Presentation titled “Genetic variants within *JAZF1* are associated with differential binding of androgen receptor, altered mRNA expression, and risk of prostate cancer” at the 11th Annual NCI Center for Cancer Research Fellows and Young Investigators Colloquium in Williamsburg, Virginia.

In May, **Philip R. Taylor, M.D., Sc.D.**, Genetic Epidemiology Branch (GEB), gave a talk on “Chemoprevention strategies for esophageal cancer” at the NCI Gastric and Esophageal Cancer Meeting in Bethesda, Maryland. In July, he spoke on “Clinical interventions: Studies great and small” at the NCI Principles and Practice of Cancer Prevention and Control Course in Bethesda, Maryland.

In May, **Nicolas Wentzensen, M.D., Ph.D.** (HREB), spoke on “The

gold standard of cervical disease— Limitations of colposcopy and histology” and on “Cervical screening for the future and the role of primary HPV screening” at the Belgian Society of Cytology meeting at the University of Antwerp in Belgium.

In May, **Xiaohong Rose Yang, Ph.D., M.P.H.** (GEB), spoke on “Characterization of germline CNVs in melanoma-prone families with/without *CDKN2A/CDK4* mutations” at the 2011 annual GenoMEL (Melanoma Genetics Consortium) meeting in Tel Aviv, Israel. In June, Dr. Yang gave a talk on “Identifying etiologic heterogeneity of melanoma and breast cancer using new technologies” at Lund University in Sweden.

DEMETRICE JORDAN MEETS THE SURGEON GENERAL

In July, **Demetrice Jordan**, a summer fellow with the Occupational and Environmental Epidemiology Branch, met with Dr. Regina M. Benjamin, the 18th Surgeon General of the United States Public Health Service (PHS), for an informational interview to discuss her fellowship at DCEG; career opportunities with the PHS Commissioned Corps; and the National Prevention Strategy, a comprehensive plan developed by representatives from 17 federal agencies that will help increase the number of Americans who are healthy at every stage of life. Ms. Jordan was also able to shadow Dr. Benjamin during one afternoon in August, sitting in on meetings, strategy planning, and conference calls.



Surgeon General Regina Benjamin and Demetrice Jordan.

COMINGS...GOINGS



Hannah Arem

Hannah Arem, M.H.S., joined the Nutritional Epidemiology Branch (NEB) as a predoctoral research fellow under the Yale University-NCI

Partnership Training Program. In NEB, Ms. Arem will be working with **Rachael Stolzenberg-Solomon, Ph.D., M.P.H., R.D.**, on dietary and obesity-related risk factors for pancreatic cancer incidence and survival. She will also be advised by Yale mentors Dr. Susan Mayne and Dr. Melinda Irwin.

Bryan Bassig, M.P.H., left the Occupational and Environmental Epidemiology Branch (OEEB) to pursue a doctoral degree in epidemiology through the Yale University-NCI Partnership Training Program. After completing his course work at Yale, Mr. Bassig will return to OEEB in 2012 to carry out his doctoral research.

Samsiddhi Bhattacharjee, Ph.D., left the Biostatistics Branch (BB) to join the National Institute of Biomedical Genomics in Kalyani, India, as an assistant professor.

Kelly Bolton, Ph.D., an NIH-Oxford-Cambridge Scholar, received her doctoral degree from Oxford University, United Kingdom, based on research conducted in collaboration with mentors at Oxford and DCEG's Laboratory of Translational Genomics (LTG). Dr. Bolton is a student in the medical school of the University of California, Los Angeles, and will be returning to that institution to complete her rotations.

Dianna Buckettt left the Infections and Immunoepidemiology Branch (IIB) to enter a master's program in molecular microbiology and immunology at Johns Hopkins University in Baltimore, Maryland.



Victoria Burton

Victoria Burton joined the Genetic Epidemiology Branch (GEB) as a postbaccalaureate fellow. She received a B.S. in molecular biology

from the University of California, San Diego. Under the mentorship of Stephen Hewitt, M.D., Ph.D., Laboratory of Pathology, NCI Center for Cancer Research, and **Philip R. Taylor, M.D., Sc.D.** (GEB), Ms. Burton will work at the Advanced Technology Center in the Tissue Array Research Program. She will investigate differential protein expression in tumors of esophageal squamous cell carcinoma patients from Shanxi Province, a region in China where rates of this tumor are very high.



Michael Cook

Michael B. Cook, Ph.D., Hormonal and Reproductive Epidemiology Branch, has been promoted from research fellow to tenure-track

investigator. Dr. Cook received a Ph.D. in molecular epidemiology from the University of Leeds, United Kingdom, in 2006; joined DCEG as a postdoctoral

fellow in 2007; and became a research fellow in 2008. Dr. Cook's research interests include the epidemiology of esophageal adenocarcinoma and its precursor, Barrett esophagus; the etiology of testicular and prostate cancer; and sex differences in cancer pathogenesis.

Naomi Frank left LTG after completing her postbaccalaureate fellowship. She will pursue a Ph.D. in genetics at the University of California, Davis.

Stephanie George, Ph.D., left NEB to join the Applied Research Program in the NCI Division of Cancer Control and Population Sciences. Dr. George's research will focus on energy balance and the epidemiology of cancer survivorship, with attention to prognosis, cancer-related comorbidities, and measurable biological factors that predict survival.



Erin Hall

Erin C. Hall, M.D., M.P.H., joined IIB as a special volunteer. Dr. Hall received her M.D. from Stanford University School of

Medicine in Palo Alto, California, and her M.P.H. from Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. She is currently on leave from a general surgery residency to conduct research regarding outcomes of solid organ transplantation. Dr. Hall will be working with **Eric A. Engels, M.D., M.P.H.** (IIB), to evaluate the cumulative incidence of cancer and to assess the effects of induction immunosuppression on cancer risk among organ recipients.



Abdisamad Ibrahim

Abdisamad Ibrahim joined LTG as a post-baccalaureate fellow under the mentorship of **Laufey Amundadottir, Ph.D.** Mr. Ibrahim

obtained his B.S. with honors in genetics, cell biology, and development at the University of Minnesota, Twin Cities. At LTG, he will be working on the functional characterization of single nucleotide polymorphisms associated with increased risk of pancreatic cancer in chromosome 13q22.1.



Kathryn Kapinos

Kathryn Kapinos was promoted to an administrative officer in the Administrative Resource Center (ARC) in June. She will provide

administrative and budget support to the Clinical Genetics Branch (CGB), the Office of Education (OE), and the Office of Communications and Special

Initiatives (OCSI). Ms. Kapinos started with the ARC as a part-time student in May 2007. In December 2007, she graduated from the University of Maryland, College Park, with a B.A. in psychology and became a full-time administrative technician, supporting the work of three senior administrative officers in the DCEG ARC.



Christopher Kim

Christopher Kim, M.P.H., joined OEEB as a predoctoral fellow. Mr. Kim received his M.P.H. in epidemiology and environmental health

from Boston University in Massachusetts and is currently enrolled in the Yale University-NCI Partnership Training Program to pursue a doctoral degree in cancer epidemiology. Under the mentorship of **H. Dean Hosgood, III, Ph.D.**, **Qing Lan, M.D., Ph.D., M.P.H.**, and **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, all of OEEB, and Dr. Yawei Zhang of Yale University, Mr. Kim will investigate molecular markers and interactions between genetic variation and air toxins in relation to lung cancer.

Jane Kim left LTG after completing her postbaccalaureate fellowship. She will attend medical school at the University of California, San Francisco.



Christine Kiruthu

Christine Kiruthu joined IIB as a pre-CRTA (Cancer Research Training Award) Fellow, following an internship with **Demetrius**

Albanes, M.D., and **Jacqueline Major, Ph.D.**, in NEB as part of the Introduction to Cancer Research Careers Program. Ms. Kiruthu has a B.S. in chemistry from the University of Maryland Eastern Shore in Princess Anne. While at IIB, Ms. Kiruthu will conduct research on Burkitt lymphoma under the mentorship of **Sam M. Mbulaiteye, M.D.**

Victoria Landsman, Ph.D., left BB to work as a biostatistician at the Centre for Global Health Research, which is sponsored by St. Michael's Hospital and the University of Toronto, Canada.

Tess Lee left OE after three years as a program assistant. She will complete her

NIH-WELLCOME TRUST FELLOW RETURNS TO DCEG

In April, DCEG welcomed returning NIH-Wellcome Trust Fellow **Lauren Houghton, M.Sc.**, to the Epidemiology and Biostatistics Program (EBP). Ms. Houghton received her M.Sc. in biological anthropology from Durham University in the United Kingdom and was awarded the NIH-Wellcome Trust Fellowship in 2008. That same year, Ms. Houghton spent the first two months of her fellowship with DCEG before returning to Durham University to begin her doctoral training.

For the past two years, Ms. Houghton has been conducting fieldwork with more than 500

school-aged girls living in London, England, or Sylhet, Bangladesh, to gather biospecimens and ethnographic data. Her dissertation research, titled the *Adolescence among Bangladeshi and British Youth (ABBY) Project*, explores associations between early-life environment and risk of breast cancer by investigating hormonal variation before puberty among Bangladeshi girls and British girls of white or Bangladeshi descent. Throughout her fellowship, Ms. Houghton has worked with **Robert N. Hoover, M.D., Sc.D.**, Director of EBP, and other mentors in DCEG, along with her mentors from Durham University, Ms. Gillian Bentley, Dr. Mark Booth, and Dr. Kate Hampshire.

More information about the NIH-Wellcome Trust Fellowship is available online at <http://go.usa.gov/939> (case sensitive).



Lauren Houghton

degree in nursing from the Washington Adventist University in Takoma Park, Maryland, and will later work at the Children's National Medical Center in Washington, D.C.



Paige Maas

Paige Maas joined BB as a predoctoral fellow. Ms. Maas graduated from Pomona College in Claremont, California, with a B.A. in

applied mathematics, and she is currently a second-year doctoral student in the Biostatistics Department at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. She will be working with **Nilanjan Chatterjee, Ph.D.**, Chief of BB, and **Mitchell H. Gail, M.D., Ph.D.** (BB), on developing absolute-risk models for specific breast cancer subtypes.



Carl McCabe

Carl McCabe, Ph.D., joined the Office of Division Operations and Analysis as a scientific program specialist. Dr. McCabe will

serve as the lead project officer on the Biomedical Computing Support contract, currently held by Information Management Services, Inc. He will also serve as administrator of DCEG's Internet presence (both internal and public facing) and will lead the management of scientific data integration for the Division. Dr. McCabe received his Ph.D. in anthropology from the University of California, Davis. His doctoral work included ethnographic fieldwork in Beijing, China, and software development for lab-based social science

experiments in California. He came to NIH as a Presidential Management Fellow in 2009, where he worked in the NIH Office of the Director, Office of Extramural Research.



Victoria McCallum

Victoria A. McCallum, M.P.H., joined OCSI as a technical writer and editor. She received her M.P.H. in epidemiology from

Emory University in Atlanta, Georgia, before joining NCI as a Presidential Management Fellow, where she had rotations in science communications, public health genomics, and congressional affairs. She will work with **Wendy Schneider-Levinson** (OCSI) as a writer and editor for *DCEG Linkage*. In addition, Ms. McCallum will manage and prepare reports on the Division's research portfolio, update website content, and provide support for other communications activities.

Idan Menashe, Ph.D., left BB to work as a bioinformatics scientist with MindSpec, Inc., a nonprofit organization in McLean, Virginia, that uses innovative bioinformatics strategies to accelerate research on common neurodevelopmental disorders.



Bridgett Rahim-Williams

Bridgett Rahim-Williams, Ph.D., joined IIB as a fellow from the National Institute on Minority Health and

Health Disparities. She received a Ph.D. in applied biomedical anthropology from the University of South Florida

in Tampa. While at IIB, Dr. Rahim-Williams will conduct research on Burkitt lymphoma under the mentorship of **Sam M. Mbulaiteye, M.D.**



Helen Reed

Helen Reed, M.P.H., joined CGB as a CRTA Fellow after receiving her M.P.H. from the University of California, Berkeley. Her

thesis analyzed the association between herbicides in house dust and the risk of childhood leukemia. Ms. Reed will be working with **Blanche P. Alter, M.D., M.P.H.** (CGB), on the Inherited Bone Marrow Failure Syndromes Cohort Study and with **Douglas Stewart, M.D.** (CGB), on tumors associated with neurofibromatosis type 1.

Linda Ross retired in June after six years of service as an administrative officer in the DCEG ARC and a total of 30 years of government service. She will be spending time at her beach home in Myrtle Beach, South Carolina.

Fatma Shebl, M.D., Ph.D., left IIB to become an assistant professor in chronic disease epidemiology at Yale University in New Haven, Connecticut.



Abbey Thompson

Abbey Thompson joined LTG as a postbaccalaureate fellow under the mentorship of **Laufey Amundadottir, Ph.D.** Ms.

Thompson obtained her B.S. in molecular biology at Northwestern University in Evanston, Illinois. In LTG, she will be working on functional characterization

of pancreatic cancer susceptibility loci identified by PanScan, the genome-wide association study of pancreatic cancer.



Cheng-Ping Wang

Cheng-Ping Wang, Ph.D., joined IIB as a special volunteer for a sabbatical year from his position as a clinical assistant professor of otolaryngology at the College of Medicine, National Taiwan University in Taipei, China. He will be working with **Allan Hildesheim, Ph.D.**, Chief of IIB, and others involved in studies of environmental and genetic factors related to nasopharyngeal carcinoma (NPC) in Asia and North Africa and will be involved in the evaluation of the use of Epstein-Barr virus serology and DNA testing for screening and early detection of NPC among

high-risk individuals. Dr. Wang is a long-standing collaborator on DCEG studies of NPC in high-risk multiplex families and is a co-investigator on an ongoing case-control study of NPC sponsored by the Academia Sinica in Taiwan, China.



Jianbing Wang

Jianbing Wang, Ph.D., joined NEB as a visiting fellow after completing his Ph.D. in epidemiology at the Cancer Institute and Hospital of the

Chinese Academy of Medical Sciences in Beijing. In NEB, he will work with **Sanford M. Dawsey, M.D.**, to complete a 25-year follow-up analysis of the Linxian Dysplasia Trial intervention and analyses of the association of vitamin D and liver cancer in the Linxian General Population Trial.

Ingrid Wentzensen, M.D., left CGB to join the Medical Genetics Fellowship program at Johns Hopkins University in Baltimore, Maryland.



Han Zhang

Han Zhang, Ph.D., joined BB as a visiting fellow. He received a Ph.D. in statistics from the University of Science and Technology of

China in Hefei. Under the mentorship of **Kai Yu, Ph.D.** (BB), Dr. Zhang will conduct research in statistical genetics, addressing challenges arising from the study of rare genetic variants and pathway analysis. He is also interested in applying data-mining approaches to explore large-scale epidemiology studies.

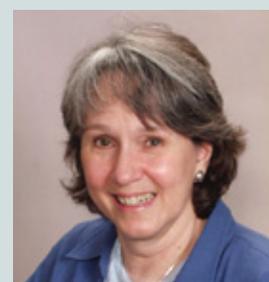
MARY FRASER, PIONEERING RESEARCH NURSE, RETIRES

Mary C. Fraser, R.N., M.A., a research nurse specialist in the Genetic Epidemiology Branch (GEB), recently retired after 34 years at NCI. Ms. Fraser earned her R.N. from the Western Pennsylvania Hospital in Pittsburgh, a B.S.N. from Pennsylvania State University, and her master's in nursing from New York University. She joined the NIH Clinical Center as a nurse in 1977, and in 1979, she transferred to the cancer epidemiology and genetics research program to focus on studies of individuals and families at high risk of cancer. Ms. Fraser also served as a commissioned officer in the U.S. Public Health Service from 1979 to 2007, earning numerous awards, including the prestigious Chief Nurse Officer Award for her service and achievements during this time.

Ms. Fraser has been a pioneer in developing the role of oncology nurses in the care and education of members of cancer-prone families and other high-risk individuals. She is internationally known for her expertise in familial cancer, particularly melanoma. She has been a leader in educating

nurses and the medical community about the risks of multiple primary cancers, including treatment-induced cancers. She was awarded the Oncology Nursing Society (ONS) Excellence in Publication Award for Clinical Practice for her work in this area. She has also served as an important liaison between the leadership of ONS and the Dermatology Nurses' Association. In this role, she has advocated for more clinical responsibility for dermatology nurses, similar to the important roles that oncology nurses serve. She was a member of the National Council on Skin Cancer Prevention for almost a decade and of the American Academy of Dermatology Melanoma/Skin Cancer Committee.

For many years, Ms. Fraser was the primary nurse for all clinical studies in DCEG's epidemiology and genetics program. As the range and number of families increased over time, she focused mainly on melanoma-prone families while still overseeing all family studies. She spent many years counseling and educating members of melanoma-prone families that were participating in GEB's research



Mary Fraser

studies. In addition to assisting with clinical examinations, she counseled participants on ways to reduce their risk of melanoma and how to recognize

dysplastic nevi and other warning signs of early-stage melanoma. "It was truly gratifying to be involved with these families over many years," she remarked.

With the recent DCEG advances in understanding the susceptibility genes for melanoma, Ms. Fraser has incorporated that information into her counseling efforts and has emphasized to patients and their families the great contributions they have made in helping to advance knowledge about the causes and control of melanoma.

FRAUMENI INDUCTED INTO THE AMERICAN ACADEMY OF ARTS AND SCIENCES

In October, DCEG Director **Joseph F. Fraumeni, Jr., M.D.**, was inducted into the American Academy of Arts and Sciences in Cambridge, Massachusetts. The Academy's members include some of the world's most accomplished leaders from academia, business, public affairs, the humanities, and the arts.

Since it was founded in 1780 by John Adams, James Bowdoin, John Hancock, and other scholar-patriots, the Academy has served as both an honorary society and a leading center for independent policy research. Its members have included George Washington and Benjamin Franklin in the 18th century, Daniel Webster and Ralph Waldo Emerson in the 19th century, and Albert Einstein and Winston Churchill in the 20th century. The current membership comprises more than 250 Nobel laureates and more than 60 Pulitzer Prize winners. This year's 212 inductees included two other NIH scientists, Gisela T. Storz, Ph.D., of the *Eunice Kennedy Shriver* National Institute of

Child Health and Human Development, and Okihide Hikosaka, M.D., Ph.D., of the National Eye Institute, as well as jazz musician Dave Brubeck, documentary filmmaker Kenneth L. Burns, actor Daniel Day-Lewis, musician Bob Dylan, Dean of Harvard School of Public Health Julio Frenk, actor Helen Mirren, and singer-songwriter Paul Simon.

In recognition of his epidemiologic and multidisciplinary research into the environmental and genetic determinants of cancer, Dr. Fraumeni has received many honors, most recently the Lifetime Achievement Award from the American



Joseph Fraumeni being inducted into the American Academy of Arts and Sciences at Sanders Theatre, Harvard University.

Association for Cancer Research and the Medal of Honor from the American Cancer Society. Dr. Fraumeni also is an elected member of the National Academy of Sciences, the Institute of Medicine, and the Association of American Physicians. ■



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