National Cancer Institute

Linkage

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GWAS: Toward a Comprehensive Understanding of Cancer Causation

Genome-wide association studies (GWAS) have proven to be a valuable tool for uncovering the heritable component of cancer etiology. Emerging technologies have enabled researchers to interrogate the entire genome with relative ease, allowing for the identification of hundreds of new and unexpected associations that relate regions of the genome to disease risk. Investigators are increasingly able to pinpoint the genetic variants through resequencing and fine mapping, and then to pursue in-depth research into the functional and biological mechanisms underpinning the inherited genetic variation. The findings may eventually inform clinical studies aimed at risk prediction, early detection, and preventive or therapeutic interventions, as well as epidemiologic and statistical studies into gene-gene and gene-environment interactions aimed at a more complete understanding of cancer causation and progression.

In a recent example of groundbreaking post-GWAS research, **Meredith Yeager, Ph.D.,** Core Genotyping Facility (CGF), **Stephen J. Chanock, M.D.,** Director of CGF and Chief of DCEG's Laboratory of Translational Genomics, and Dr. Hong Lou and Dr. Michael Dean from the Center for Cancer Research (CCR) led one of the first studies to uncover the mechanisms relating a common genetic variant to prostate cancer (Lou H., et al. *Proceedings of the National Academy of Sciences* 2009;106(19):7933–7938). The study used fine mapping analysis of prostate

DCEG Authors: Amy Hutchinson, Meredith Yeager, Demetrius Albanes, Jesus Gonzalez-Bosquet, Stephen Chanock, Kevin Jacobs, Sholom Wacholder, Robert Hoover, and Stephanie Weinstein. (Not shown: Kai Yu, Nilanjan Chatterjee, Margaret Tucker, Joseph Fraumeni, and Gilles Thomas.)

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DCEG *Linkage*

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cancer cases and controls from the NCI Cancer Genetic Markers of Susceptibility (CGEMS) project to confirm two independent GWAS that identified an association between a single-nucleotide polymorphism (SNP), rs10993994, on chromosome 10q11.2 with prostate cancer risk. The SNP is located in a region that plays a role in the expression of the *MSMB* gene, which codes for a protein implicated as a potential biomarker for prostate cancer and which may act as a tumor suppressor.

In follow-up functional analyses, the investigators explored how the two variants of the SNP, found either as a thymine (T) allele or a cytosine (C) allele, influence *MSMB* expression. Compared to the T allele, the C allele was associated with greater *MSMB* expression (see Figure 1). Previous studies have shown that as prostate cancer develops from early to late stages, *MSMB* expression progressively decreases. The T allele also has been found to be more common in prostate cancer patients than in controls. Further analysis revealed that the transcription factor CREB—a protein that plays a role in initiating gene expression—binds strongly to the C allele but does not bind to the T allele. No other SNP within the *MSMB* region showed significant functional associations with the gene, though further study is needed to investigate this region more comprehensively.

The intent of the DCEG-CCR working group is to capitalize on new research opportunities derived from GWAS by promoting innovative studies that use cutting-edge genomic technologies to elucidate the genetic pathways of carcinogenesis that may be amenable to clinical intervention.

In regard to these findings, Dr. Yeager stated, "We were fortunate that the SNP identified by the GWAS was the same variant that influences the expression of *MSMB,* which is also a good candidate gene for prostate cancer. It is likely that other regions of the genome related to prostate cancer through GWAS will require much more time and effort to elucidate. We believe our findings illustrate an approach to how post-GWAS studies may be conducted."

This study models some of the goals outlined in recent NCI and National Human Genome Research Institute (NHGRI)-sponsored workshops on the current status and future directions in GWAS, which generate huge amounts of data. With the advent of increased technological capabilities, GWAS findings have grown dramatically. There are now close to 400 new regions in the genome associated with more than 75 different diseases and traits, all of which can be further explored through follow-up studies. Investigators subsequently gathered to discuss how to best manage, analyze, and pursue the vast number of associations resulting from GWAS.

"Once a GWAS signal is conclusively established, the next steps forward may be long and arduous, and require a stepwise approach to localize the common and rare variants that may be lurking in these regions," explained Dr. Chanock,

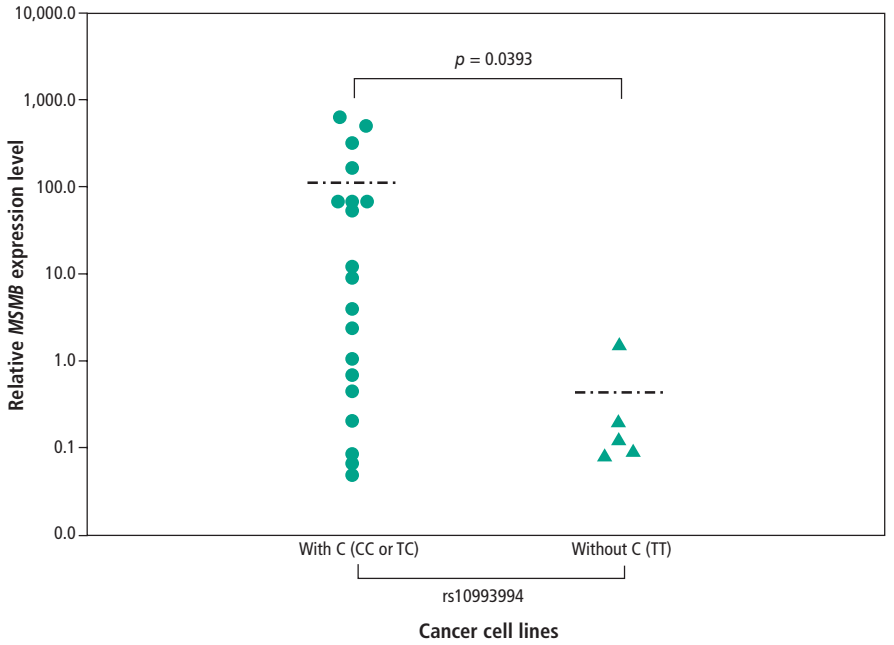


Figure 1. Distribution of *MSMB* mRNA expression relative to with or without C at single-nucleotide polymorphism rs10993994. (Lou H, et al. 2009)

who co-led the workshop on sequencing and post-GWAS research.

Many newly identified regions do not readily point to genes with known functions, and they often arise in so called "gene deserts." Follow-up studies, including fine mapping, deep sequencing, and functional analysis, are critical for analyzing the contribution of identified regions to the risk of disease and investigating whether SNPs discovered by GWAS represent the functional genetic variant or simply tag the true variants, which may be located nearby in the same haplotype. Furthermore, growing evidence shows that SNPs are not the only variation playing a role in cancer etiology. For example, researchers are now investigating the role of copy number variants, which are stretches of genomic sequence that are deleted or duplicated in varying degrees. These also may influence gene expression.

To facilitate NCI's trans-divisional collaborations aimed at refining and interpreting GWAS findings, DCEG and CCR have formed the Human Genetics and Genomics Working Group, cochaired by **Margaret A. Tucker, M.D.,** Director of the Human Genetics Program and Chief of the Genetic Epidemiology Branch; Dr. Curtis Harris, Laboratory of Human Carcinogenesis, CCR; and Dr. Mary Carrington, Laboratory of Experimental Immunology, CCR. The intent of the DCEG-CCR working group is to capitalize on new research opportunities derived from GWAS by promoting innovative studies that use cutting-edge genomic technologies to elucidate the genetic pathways of carcinogenesis that may be amenable to clinical intervention.

Dr. Tucker explained, "There is an increasing need for genetic and molecular epidemiologists to work closely with basic and clinical scientists in search of the biological consequences of genetic variants associated with cancer risk. The goal of our working group is to foster transdisciplinary projects by developing communication tools linking DCEG and CCR scientists, promoting collaborative research infrastructure and training programs, and encouraging outreach to extramural scientists and companies actively engaged in the development and application of genomic technologies."

In addition, the working group has recently established funding opportunities for collaborative studies involving DCEG and CCR investigators to follow up on validated genetic loci revealed by GWAS or by linkage analyses of cancer-prone families. DCEG and CCR jointly fund proposals up to $100,000 per year, awarded for a maximum of two years per project. All proposals are peer reviewed and ranked by members of the working group and the Steering Committee of the NCI Center of Excellence in Integrative Cancer Biology and Genomics. Each proposal is reviewed for scientific merit, innovation and novelty of the approach, feasibility, potential clinical and public health impact, and evidence of interdivisional collaboration. To date, three projects have been funded through this mechanism, with final approval by the scientific directors of DCEG and CCR.

Approval has also been received to establish a postdoctoral fellowship program that features joint research at DCEG and CCR. "By working with scientists across the intramural program, we hope to train the next generation of transdisciplinary scientists who will contribute novel insights into the genetic component of cancer. It seems likely that these insights will inform the development of new measures aimed at cancer prevention, detection, and treatment," stated Dr. Tucker. ■

—Cherie M. Vitartas, M.P.H.

DCEG HOSTS VISITING SCHOLAR WILLIAM BLOT

DCEG was honored to welcome back Dr. William Blot as a Visiting Scholar in May. Dr. Blot is associate director of Cancer Prevention, Control, and Population-based Research at the Vanderbilt-Ingram Cancer Center and professor of medicine at the Vanderbilt University School of Medicine. He also serves as the chief executive officer of the International Epidemiology Institute in Rockville. As a member of DCEG from 1974 to 1994 and as Chief of the Biostatistics Branch (BB) starting in 1984, Dr. Blot was instrumental in shaping the Division's research portfolio, identifying environmental causes of cancer through studies conducted in the United States, China, Italy, and elsewhere.

Mitchell Gail, William Blot, and Joseph Fraumeni.

While at NCI, he contributed to the development of the U.S. cancer atlases and led a series of seminal case-control studies in high-risk areas of the country that were identified by the cancer mapping project. These studies helped clarify the role of demographic, occupational (e.g., asbestos, arsenic), dietary, and other lifestyle factors (e.g., smoking, smokeless tobacco, obesity, alcohol consumption) in cancers of the oral cavity and pharynx, esophagus, stomach, pancreas, lung, kidney, bladder, and other sites. Pursuing these strategies in China, he collaborated with Chinese scientists to launch a series of case-control studies and clinical trials in high-risk areas to elucidate the effects of indoor air pollution (lung cancer), *Helicobacter pylori* infection (stomach cancer), and dietary insufficiencies (esophageal cancer).

Dr. Blot currently leads the Southern Community Cohort Study (SCCS), which is supported by several institutions, including NCI and the T.J. Martell Foundation. Researchers are continuing to register participants with the intent of creating one of the largest epidemiologic studies to explore racial disparities in cancer incidence and mortality, with a particular emphasis on the excess risks of cancer experienced among the African American population.

At the start of his two-day visit to DCEG, Dr. Blot presented a seminar titled "Examining cancer disparities: The SCCS." **Mitchell H. Gail, M.D., Ph.D.** (BB), introduced Dr. Blot, remarking that "throughout his career, Dr. Blot has identified key etiologic issues and pursued them with all the tools of epidemiology. Along the way, he created a legacy of investigational data sources, biospecimens, and ideas that benefited those around him. He continues to do that today with the establishment of the SCCS."

Dr. Blot detailed the research objectives of the eight-year-old cohort, highlighting the participation of traditionally underrepresented groups. He presented trends in cancer incidence and survival by race and gender, using data from the 150 community health centers involved in the cohort. Dr. Blot also discussed the challenges of recruitment that are unique to the study population.

Following the seminar, **Joseph F. Fraumeni, Jr., M.D.,** Division Director, presented Dr. Blot with the DCEG Visiting Scholar Award in recognition of his major achievements in the field of cancer epidemiology and public health. Dr. Fraumeni applauded Dr. Blot's fundamental contributions to DCEG and quipped, "Dr. Blot dug the wells from which we now drink." Dr. Fraumeni also remarked, "We are grateful for this opportunity to recognize Dr. Blot's efforts that continue to allow research opportunities worldwide."

As former Chief of BB, Dr. Blot joined the branch members at lunch for a lively discussion of epidemiologic and statistical issues in studies of cancer etiology. Topics included evaluating dose-response trends, choosing appropriate comparison groups, and interpreting data when multiple comparisons have been made.

Dr. Blot participated in two afternoon seminars. The first, hosted by **Ann W. Hsing, Ph.D.,** Hormonal and Reproductive Epidemiology Branch, focused on health disparities and cancer. Participants discussed cancer heterogeneity, recruitment challenges, the U.S. Kidney Cancer Study, and geographic information systems as tools to identify lifestyle and environmental risk factors.

The other seminar, hosted by **Qing Lan, M.D., Ph.D., M.P.H.,** Occupational and Environmental Epidemiology Branch (OEEB), and **Martha S. Linet, M.D., M.P.H.,** Chief of the Radiation Epidemiology Branch, focused on etiologic and intervention studies in China. Ongoing projects discussed included investigations of the hematotoxicity of benzene and the risk of lung cancer in relation to indoor smoke from coal combustion.

Dr. Blot posed questions and offered feedback throughout the sessions.

The next morning Dr. Blot attended a DCEG women scientists' breakfast, followed by a meeting on diet and cancer led by Nutritional Epidemiology Branch investigators **Yikyung Park, Sc.D.,** and **Amanda J. Cross, Ph.D.** Presenters from DCEG and the Division of Cancer Control and Population Sciences focused on new tools for dietary and physical activity measurements in cohort studies.

Wong-Ho Chow Ph.D. (OEEB), and **Philip R. Taylor, M.D., Sc.D.,** Genetic Epidemiology Branch (GEB), moderated a session highlighting studies of cancer of the upper gastrointestinal tract. Participants reviewed initial findings from the BEACON (Barrett's Esophagus and Adenocarcinoma Consortium), which is pooling data on such risk factors as obesity, smoking, gastroesophageal reflux, alcohol consumption, and non-steroidal anti-inflammatory drugs.

DCEG fellows had the opportunity to discuss career paths for epidemiologists with Dr. Blot during a brown bag lunch. He encouraged the fellows to work across different sectors, highlighting his experience in government, private, and academic research institutions.

GEB investigators **Neil E. Caporaso, M.D.,** and **Maria Teresa Landi, M.D., Ph.D.,** hosted the final session on new directions in lung cancer etiology. They discussed results from the EAGLE (Environment and Genetics in Lung Cancer Epidemiology) study on genetic determinants of lung cancer and smoking propensity, and they sought Dr. Blot's input on these exciting new findings.

About his visit, Dr. Blot commented, "It was a great pleasure for me to return to NCI for discussions with colleagues, many of whom I have known for years, about the causes, prevention, and control of cancer." ■

—Hannah Arem, M.H.S.

SPRING 2009 INTRAMURAL RESEARCH AWARDS

DCEG Intramural Research Awards (IRAs) are competitive funding opportunities designed to encourage innovative, interdisciplinary research by fellows and tenure-track scientists. The IRA program includes spring and fall cycles, with up to three proposals funded per cycle.

Shahinaz Gadalla, Dean Hosgood, and Ying Gao.

The winners of the spring 2009 competition were **Shahinaz M. Gadalla, M.D., Ph.D.,** a cancer prevention fellow in the Clinical Genetics Branch, for her proposal "Donor and recipient telomere length as predictors of outcomes after hematopoietic stem cell transplant in patients with acquired severe aplastic anemia"; **Ying Gao, M.D., Ph.D.,** Genetic Epidemiology Branch, for "Gene-specific methylation in colorectal carcinogenesis in the PLCO (Prostate, Lung, Colorectal and Ovarian) Study"; and **H. Dean Hosgood, III, Ph.D.,** Occupational and Environmental Epidemiology Branch, for "Relation of combustion-derived nanoparticle exposure to inflammation and oxidative stress."

Members of the NCI Board of Scientific Counselors and senior DCEG scientists reviewed the proposals. They were judged on their potential for significant scientific and public health impact, innovation, interdisciplinary nature, ability to achieve the objectives within the proposed time frame and resources, and relevance to the mission of the Division.

WILLIAM ANDERSON UNITES CLINICAL PERSPECTIVE WITH CANCER RESEARCH

William F. Anderson, M.D., M.P.H., Biostatistics Branch (BB), has a perspective borne of 20 years as a community-based hematologist/medical oncologist in Monroe, Louisiana, where his experience and passion for uncovering the causes of cancer steered him toward a career in population-based research with DCEG. Dr. Anderson says his path was not "well calculated," yet a certain logic and inevitability seem apparent when you speak with him.

Dr. Anderson is board-certified in internal medicine, hematology, and medical oncology. After receiving his training at Tulane University School of Medicine in New Orleans, he planned to spend approximately six months in the medically underserved northeast part of Louisiana before proceeding with a postgraduate leukemia research fellowship in Seattle. Six months became 16 years, but it was here that he developed his interests in cancer etiology, preventive oncology, cancer surveillance research, and public health.

He subsequently arrived at NCI in 1998 as a Cancer Prevention Fellow. As part of the fellowship, he obtained an M.P.H. degree in epidemiology at the Tulane University School of Public Health and Tropical Medicine. "I naively thought I was extending my private practice experience," he says, "but instead had to learn many new skills." He then began to work with NCI's Surveillance, Epidemiology, and End Results (SEER) database, often in collaboration with DCEG investigators, including **Nilanjan Chatterjee, Ph.D.,** Chief of BB; **Louise A. Brinton, Ph.D.,** Chief of the Hormonal and Reproductive Epidemiology Branch (HREB); **Mark E. Sherman, M.D.** (HREB); and **Susan S. Devesa, Ph.D.** (BB).

"The quantitative mentoring and the collaboration that I have found within DCEG have been integral to my research."

When a tenure-track investigator position opened in BB in 2005, Dr. Anderson saw an opportunity for his descriptive epidemiology work to become more quantitative. He was impressed with the Division's dedication to high-quality research. Emphatically he says, "The quantitative mentoring and the collaboration that I have found within DCEG have been integral to my research."

William Anderson

Working with BB senior investigators, such as Dr. Chatterjee, **Mitchell H. Gail, M.D., Ph.D., Ruth M. Pfeiffer, Ph.D.,** and **Philip S. Rosenberg, Ph.D.,** Dr. Anderson has been able to apply a rigorous biomathematical approach and a clinical perspective to cancer surveillance research and descriptive

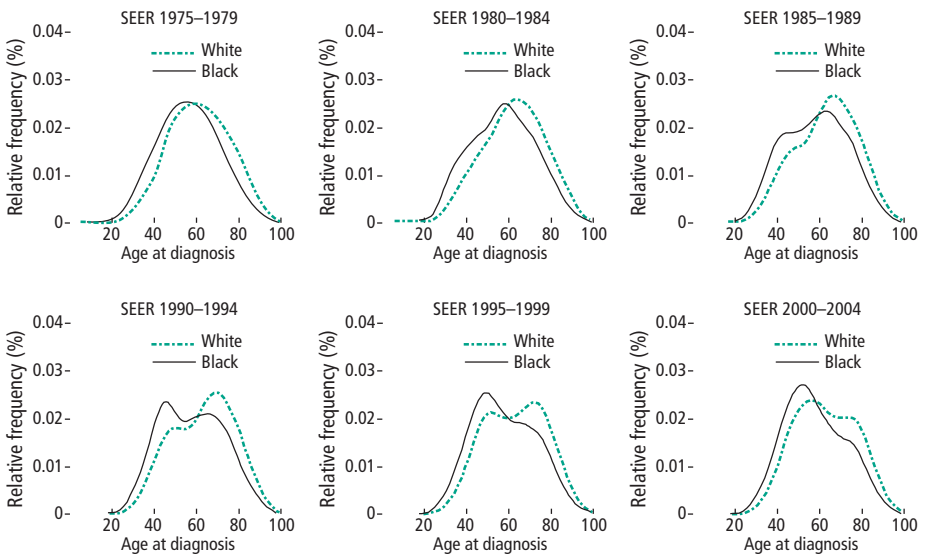


Figure 1. Age distributions at diagnosis by race (black versus white) and time period (1975–1979, 1980–1984, 1985–1989, 1990–1994, 1995–1999, and 2000–2004) in NCI's Surveillance, Epidemiology, and End Results (SEER) 9 Registries database. (Anderson WF, et al. 2008)

epidemiology. In all his endeavors, he is committed to looking at his data "agnostically," not wedded to any *a priori* hypotheses. According to Dr. Anderson, good descriptive studies should be thoughtful and provocative; they test old ideas and generate new hypotheses.

In addition to analyzing SEER's public-use database, Dr. Anderson also is exploring SEER's "value-added" Residual Tissue Repository (RTR) by conducting studies that merge molecular biology with population-based concepts and analytical techniques. In 2007, he received funding through the NCI Director's Intramural Innovation Award to use the RTR to examine population-based incidence rates for molecular subtypes of breast cancer. In 2009, he received an NIH Merit Award for providing new insights into cancer etiology through descriptive studies of cancer heterogeneity and racial disparities.

Dr. Anderson was recently chosen to be the founding senior editor of a new manuscript section, "Cancer Surveillance Research," in the journal *Cancer Epidemiology, Biomarkers & Prevention*. He is enthusiastic about this undertaking, believing that surveillance studies are a valuable resource for cancer research. "Evaluation of cancer rates can provide clues to cancer etiology, which can then generate hypotheses to be tested in clinical trials or through analytic studies," explained Dr. Anderson. "Once a hypothesis has been proven valid, it should then be assessed to determine if it is effective in the general population." It is through this method that researchers can determine whether clinically validated preventive or therapeutic measures are practical in application.

"Evaluation of cancer rates can provide clues to cancer etiology, which can then generate hypotheses to be tested in clinical trials or through analytic studies."

When asked if he misses working with patients, Dr. Anderson admits that he loved his patients and fully expected to return to private practice. He has since realized, however, that he can still affect patient care through independent research, collaborations, and mentoring. Ultimately, he hopes that "this type of work will help to bring all the pieces together and make a coherent story to inform cancer treatment and prevention." ■

—Rebecca Razavi

DRS. LINET AND HARTGE RECOGNIZED BY THE INTERLYMPH CONSORTIUM

The International Consortium of Investigators Working on Non-Hodgkin Lymphoma Epidemiology Studies, referred to as InterLymph or the InterLymph Consortium, honored **Martha S. Linet, M.D., M.P.H.,** Chief of the Radiation Epidemiology Branch, and **Patricia Hartge, Sc.D.,** Epidemiology and Biostatistics Program, at the InterLymph 2009 Annual Scientific Meeting in Vancouver. The consortium members presented Drs. Linet and Hartge with Awards for Outstanding Service in recognition of their insight, initiative, and key roles in founding InterLymph. Both have served in the governing group, on working panels devoted to specific projects, and as authors on reports of pooled analyses conducted by the consortium.

Founded in 2001, InterLymph has served as an open scientific forum for epidemiologic research on non-Hodgkin lymphoma. Supported by DCEG, the Division of Cancer Control and Population Sciences, the International Agency for Research on Cancer in Lyon, France and the Leukemia Research Fund in London, the international consortium consists of investigators who have completed or who have ongoing case-control studies of lymphoma and who undertake large-scale collaborative research projects that pool data across the individual studies.

Patricia Hartge and Martha Linet.

RUTH KLEINERMAN STUDIES RADIATION AND SECOND CANCERS

"Finding the first clear evidence of the gene-environment interactions underlying the excess risk of secondary cancers in patients with retinoblastoma has been a most gratifying accomplishment," says **Ruth A. Kleinerman, M.P.H.,** an epidemiologist with the Radiation Epidemiology Branch (REB). She has reason to celebrate: this year marks her 30th anniversary with NCI and 30 years of extraordinary productivity in cancer research. Using the collaborative approach that is the linchpin of successful epidemiologic studies, she has established risk factors for several forms of cancer.

Ms. Kleinerman's work has been featured in more than 100 articles published in peer-reviewed journals. Not only has she been the recipient of both group and individual NIH Merit awards, but she also has twice received the DCEG Award for Outstanding Research Paper by a Staff Scientist. Perhaps her greatest achievement, however, has been her major discoveries in ophthalmic oncology.

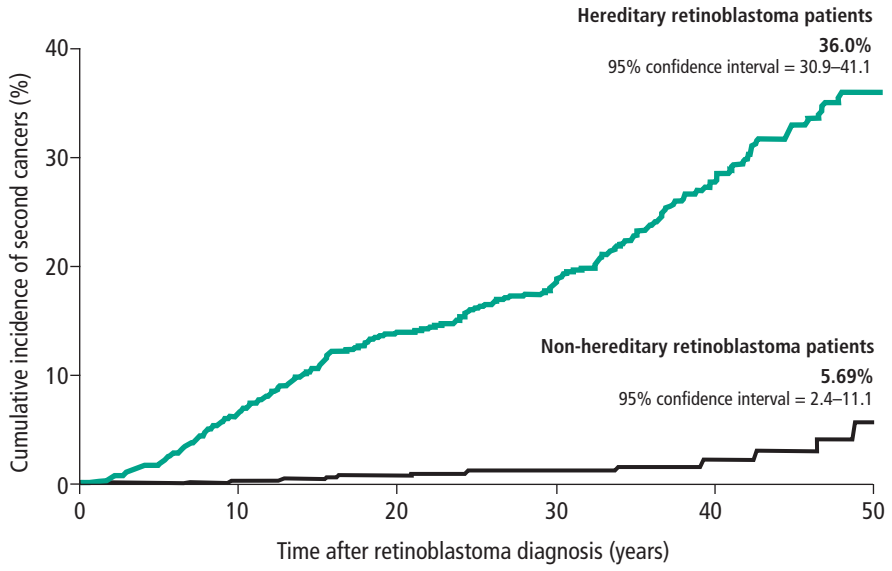
Retinoblastoma, a cancer that develops in the tissues of the retina, usually occurs in children younger than five years of age and can be either hereditary or nonhereditary (i.e., sporadic). Children with retinoblastoma have excellent survival rates, up to 97 percent at five years. However, children who survive hereditary retinoblastoma have substantially increased risks of developing second primary cancers.

Ruth Kleinerman

Ms. Kleinerman established a cohort of retinoblastoma survivors during the mid-1980s and has been following them for decades. She has found that those with the hereditary form of retinoblastoma are also at elevated risk for bone and soft tissue sarcomas, melanoma, and brain tumors due to a germline mutation in their *RB-1* gene, which encodes the cell cycle regulatory protein pRb. She observed the excess risk of secondary cancers to be primarily among children with hereditary retinoblastoma who receive radiotherapy and to persist in a dose-dependent manner throughout the adult years.

"Finding a dose-related relationship between radiation exposure and second cancers has transformed the care given to children with hereditary retinoblastoma," she explains. "The goal of treatment today is to minimize radiotherapy exposure in these patients and intensify cancer-screening efforts throughout their lives."

According to Dr. David Abramson, Chief of the Ophthalmic Oncology



Number of Patients at Risk						
Years after diagnosis	1	10	20	30	40	50
Hereditary	963	760	615	401	147	30
Non-hereditary	638	570	500	317	134	46

Figure 1. Cumulative incidence of a second cancer by time since diagnosis of retinoblastoma.

Service at Memorial Sloan-Kettering Cancer Center and a longtime collaborator, "Ms. Kleinerman's papers have dramatically changed our understanding of retinoblastoma and the way in which the disease is managed worldwide."

"Ms. Kleinerman's papers have dramatically changed our understanding of retinoblastoma and the way in which the disease is managed worldwide."

Not only does Ms. Kleinerman continue to follow the original retinoblastoma cohort, but she also has established cohorts of patients who have been treated more recently, and she is following them using innovative methods. "We are using new internet tools such as Facebook to reach out to retinoblastoma survivors who are now in their twenties. In addition, we will soon launch a Web site to seek out retinoblastoma survivors and provide screening information," Ms. Kleinerman reports. "It will be interesting to see how well social media works for contacting potential members of this cohort."

Within DCEG, Ms. Kleinerman is known for her successful collaborations, both here and abroad. She became involved in a study of families with ataxia-telangiectasia (a rare, childhood neurological disorder that causes degeneration in the part of the brain controlling motor movements and speech) using Nordic cancer registries. In 2005, she organized a joint meeting of several European groups to pursue observations of increased cancer incidence in affected families.

Among the many other interesting studies with which she has been involved was one in Gansu Province, China, where more than half the population lives underground in so-called "cave dwellings" with significantly elevated radon levels. The research team found a direct link between the risk of lung cancer and the levels of exposure measured through radon detectors. Ms. Kleinerman recounts, "I was very fortunate to have the opportunity to travel to a rural part of China and carry out research that uncovered a very clear health risk to residents living within the area."

Still in the beginning stages is a study of cancer mortality among interventional radiologists and cardiologists. As the numbers of fluoroscopically guided procedures and higher-dose diagnostic x-ray examinations have increased over recent decades, so too have concerns about radiation exposure to patients and physicians. In collaboration with other REB investigators, Ms. Kleinerman is now assembling a cohort of specialty groups and exploring different ways of assessing their radiation exposure and subsequent risks of cancer.

Ms. Kleinerman earned her master's degree in public health at the Boston University School of Public Health and holds an undergraduate degree in art history from Washington University in St. Louis. She counts herself lucky to live in Washington, DC, where she has plenty of opportunities to indulge her love of fine art at the city's myriad art museums and galleries. ■

—Karen Eddleman

DCEG SELECTS THE FIRST ROBERT A. WELCH FELLOW

Jesus Gonzalez-Bosquet, M.D., Ph.D., Laboratory of Translational Genomics (LTG), has been selected as the first Robert A. Welch Fellow. Dr. Gonzalez-Bosquet joined LTG in 2007 and has been working with his mentor **Stephen J. Chanock, M.D.,** Chief of LTG and Director of the Core Genotyping Facility (CGF), on follow-up analyses of data from genome-wide association studies using fine mapping and deep sequencing technologies to pinpoint causal variants and determine the function of those genetic variants. The award provides Dr. Gonzalez-Bosquet with funding for additional training in his research field.

Jesus Gonzalez-Bosquet

The Robert A. Welch Fellowship is a competitive, postdoctoral award within DCEG to support mentored research in molecular epidemiology, with special emphasis on the application of emerging genetic and genomic technology. The fellowship was established in honor of the late Robert A. Welch, M.S., founding Director of Operations of CGF. Mr. Welch played a vital role in developing and guiding the CGF and its large-scale studies of the cancer risks associated with common genetic variations. His skill and dedication were critical to the success of DCEG's collaborative research program in human genetics.

—Alexandra Ekblom, M.P.H.

SALLIE ROSEN KAPLAN FELLOWS JOIN THE DIVISION

Tamra Meyer, Ph.D., and **Meredith Shiels, Ph.D.,** recently joined the Hormonal and Reproductive Epidemiology Branch (HREB) and the Infections and Immunoepidemiology Branch (IIB), respectively, as the Division's newest Sallie Rosen Kaplan Postdoctoral Fellows.

The Sallie Rosen Kaplan Fellowship for Women Scientists in Cancer Research is awarded through an annual competition for postdoctoral fellows who wish to train in the NCI Intramural Research Program. Made possible by a bequest from Ms. Kaplan to the Foundation for NIH, fellows receive a supplement to their first-year stipend.

Tamra Meyer and Meredith Shiels.

Dr. Meyer comes to HREB from the University of Texas School of Public Health in Houston, where she earned an M.P.H. in disease control and a Ph.D. in epidemiology under the guidance of Dr. Eric Boerwinkle. At DCEG, she will pursue her interests in molecular epidemiology, particularly the role of inflammation and genetic susceptibility as they relate to hormonal cancers. She is working with HREB investigator **Ann W. Hsing, Ph.D.,** in collaboration with Biostatistics Branch investigators **Kai Yu, Ph.D., Qizhai (James) Li, Ph.D., Philip S. Rosenberg, Ph.D.,** and **Idan Menashe, Ph.D.,** in applying cutting-edge statistical tools to identify the origins of prostate cancer. Toward this end, Dr. Meyer is using genome-wide association data for prostate cancer from the Cancer Genetic Markers of Susceptibility Study to evaluate gene-environment interactions in 800 inflammation-related genes, as well as serum androgen levels, using the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. She is also using data from the NIH-AARP Diet and Health Study to evaluate the relationship between the use of non-steroidal anti-inflammatory drugs and the risk of cancer.

In addition to her research in prostate cancer, Dr. Meyer is working with Dr. Hsing on the Shanghai Biliary Tract Cancer Study to assess the role of genetic and other risk factors for both biliary cancer and gallstones. "It is exciting to be a part of the DCEG team of scientists," Dr. Meyer remarked. "The environment here is ideal for fostering the collaborative science that is necessary to understand, prevent, and treat complex diseases like prostate cancer."

Dr. Shiels received her undergraduate degree in biobehavioral health from Pennsylvania State University, followed by an M.H.S. and a Ph.D. in epidemiology from the Johns Hopkins Bloomberg School of Public Health. She studied the relation of genetic variants to tobacco smoking for her master's thesis, before focusing her doctoral research on the epidemiology of cancer among people infected with human immunodeficiency virus (HIV) under the guidance of Dr. Stephen Cole.

During her postdoctoral fellowship in IIB, Dr. Shiels will pursue research relating to the role of infections, inflammation, and immunodeficiency in the development of cancer. She will continue her work on HIV-related cancers by using data from the HIV/AIDS Cancer Match Study to evaluate the overall burden of cancer among HIV-infected people in the United States. According to Dr. Shiels, "DCEG is the ideal place to build upon my doctoral research on cancer among HIV-infected individuals. I feel very fortunate to be working with investigators who are experts in the study of HIV and cancer, and to have access to data from the HIV/AIDS Cancer Match Study."

In addition, Dr. Shiels will use the PLCO study to evaluate the risk of lung cancer associated with serum markers of pulmonary fibrosis and scarring, along with genetic variants in the inflammation and innate immunity pathways.

Dr. Shiels's primary mentor is **Eric A. Engels, M.D.** (IIB); she will also work closely with **Anil K. Chaturvedi, Ph.D.,** and **James J. Goedert, M.D.,** both of IIB. ■

FOSTERING INTERDISCIPLINARY RESEARCH IN IONIZING RADIATION

The Radiation Epidemiology Branch (REB)—in collaboration with Georgetown University Medical Center, the National Institute of Allergy and Infectious Diseases, the Environmental Protection Agency, Helmholtz Zentrum München, and the European Union—funded and organized a three-day conference in May, titled Late Health Effects of Ionizing Radiation: Bridging the Experimental and Epidemiologic Divide, at Georgetown University in Washington, DC. This international conference fostered interdisciplinary research by stimulating collaboration and synergistic interactions among epidemiologists, statisticians, radiobiologists, and dosimetrists. **Elaine Ron, Ph.D.** (REB), and Dr. Peter Jacob, Helmholtz Zentrum München, cochaired the conference; **Martha S. Linet, M.D., M.P.H.,** Chief of REB, served on the organizing committee; and Dr. Albert Fornace, Georgetown University Medical Center, hosted the event. **Jenna Nober** and **Abigail Ukwuani, M.P.A.** (both in REB), along with Jennifer Donaldson (formerly of REB and now a private contractor) and Karen Howenstein (Georgetown University), coordinated the conference.

Organizing Committee: Elisabeth Cardis, Jenna Nober, Jennifer Donaldson, Julian Preston, Elaine Ron, Colin Muirhead, Martha Linet, Albert Fornace, Abigail Ukwuani, and Roy Shore. (Not shown: Peter Jacob.) *(Photograph credit: Annelie Landgren)*

Approximately 150 researchers from 11 countries participated in the conference, which featured 36 invited speakers from the fields of epidemiology, biostatistics, cell biology, radiobiology, genetics, physics, nuclear engineering, and radiation protection. Two sessions, including more than 75 posters, covered a wide range of radiation-related topics. To encourage junior investigators to pursue careers in radiation research, five travel fellowships were awarded, based on submitted abstracts.

Several REB investigators gave invited presentations. Dr. Ron spoke about radiation-related risks of non-malignant thyroid diseases, Dr. Linet reviewed cancer risks in medical radiation workers, and **Alina V. Brenner, M.D., Ph.D.** (REB), discussed the incidence of thyroid cancer following iodine-131 exposure from the Chernobyl disaster. **Amy Berrington de Gonzalez, D. Phil.** (REB), presented the risk of second solid cancers among breast cancer survivors and estimated the fraction of those cancers attributable to radiotherapy. In addition, Dr. Ron chaired a session on radiation risk and the public; **Ruth A. Kleinerman, M.P.H.** (REB), chaired one on late health effects of radiation therapy; and **Kiyohiko Mabuchi, M.D., Dr.P.H.** (REB), led a session on radiation-related cardiovascular disease.

The sessions highlighted the need to develop models to study genetic damage and repair following low-dose radiation exposures, mechanistic modeling of radiation effects, the importance of stem cell biology in understanding radiation carcinogenesis, and new methods for retrospectively quantifying radiologic procedures. Recent occupational data have suggested that the dose response for cancer risk from chronic radiation exposure is consistent with that from acute exposure and that underground miners may have an elevated risk of extrapulmonary cancers associated with radon. In response to the new interest in radiation-related, non-malignant diseases, speakers presented data on cardiovascular damage, cataracts, immune function, and thyroid diseases. The concluding talks focused on risks and benefits of computed tomography, radiation risk perception, and radiation-related communication and policy.

The conference closed with a round-table discussion, cochaired by **Alice J. Sigurdson, Ph.D.** (REB), emphasizing new directions in radiation research from the perspectives of experts in radiation oncology, epidemiology, molecular biology, and genetics. The discussion highlighted areas of mutual interest, identified gaps in knowledge, and proposed several possible future collaborations between epidemiologists and laboratory scientists to investigate further questions about radiation-related diseases. Papers from invited speakers will be published. ■

—Ruth A. Kleinerman, M.P.H., and Elaine Ron, Ph.D.

TECHNICAL EVALUATION OF QUESTIONNAIRES' CHANGING OF THE GUARD

Betty Jane (B. J.) Stone, Ph.D., a staff scientist in the Biostatistics Branch, stepped down in September as chair of DCEG's Technical Evaluation of Questionnaires (TEQ) Committee. Dr. Stone, who will retire in December after 33 years at NCI, has led TEQ for more than a decade. During her time at NCI, she has assembled and overseen a searchable collection of questionnaire modules on the DCEG intranet. This resource has proven valuable to extramural and intramural investigators. She has also served as an administrator for the NCI Atlas of Cancer Mortality. An analytic thinker with great editing skills, she has coauthored many papers on the causes of cancer among high-risk populations and edited numerous articles written by other DCEG researchers. Dr. Stone will be missed for her many substantial contributions to the Division's mission of high-quality research and training.

D. Michal Freedman, Ph.D., M.P.H., a staff scientist in the Radiation Epidemiology Branch since 1999, has been appointed as the new chair of TEQ. Dr. Freedman came to NCI in 1994 through the Cancer Prevention Fellowship Program. Previously, she received a J.D. degree from Yale and practiced law for the government, a private firm, and a public interest organization. She subsequently received an M.P.H. degree in 1995 and earned her doctorate in epidemiology in 1998 from Johns Hopkins University. Dr. Freedman's exceptional background will serve her well as she presides over a committee that not only evaluates the scientific content of questionnaires, but also examines the tone and precision of their wording.

Michal Freedman and B. J. Stone.

The TEQ provides formal review of questionnaires to be used in DCEG studies. Approval by TEQ is strongly recommended before a questionnaire is submitted to the Office of Management and Budget for clinical exemption or clearance and before use in the field. The TEQ solicits questionnaires for review once a month. Its aim is to aid investigators in developing effective questionnaires by evaluating:

- Where language might be altered to make it clearer to the average subject;
- Whether questions deal with sensitive areas, and if so, whether the subject matter is important enough to the study to risk offense;
- Whether questions or areas that are central to the subject matter have been omitted or underemphasized;
- Whether there are too many questions for a significant portion of subjects to answer (e.g., if the case subjects are seriously ill); and
- Whether there are enough questions on individual topics to permit meaningful analysis. ■

DCEG STAFF ATTEND THE SOCIETY FOR EPIDEMIOLOGIC RESEARCH MEETING

The Society for Epidemiologic Research (SER) held its 42nd annual meeting in Anaheim, California in June. The title and theme of this year's meeting was Epidemiologists as Vectors for Transmitting Health. Many DCEG researchers participated in the event by chairing sessions, giving presentations, or displaying posters of their latest research.

Louise A. Brinton, Ph.D., Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), chaired the session "Predictors of breast cancer recurrence and survival" and presented the poster "Male breast cancer in the Veterans Administration hospitalization database."
D. Michal Freedman, Ph.D., M.P.H., Radiation Epidemiology Branch, spoke on "Sunlight, hormone replacement status, and colorectal cancer risk in post-menopausal women."
Edgar Simard, M.P.H., Infections and Immunoepidemiology Branch, gave a presentation on "Spectrum of cancer risk late after AIDS in the United States." He was also selected as the president-elect of the SER Student Caucus, which fosters the academic and professional development of student participants.

Other presentations included posters by **Michael C. R. Alavanja, Dr.P.H.,** Occupational and Environmental Epidemiology Branch, "Pesticide exposure and the risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study," and **Michael B. Cook, Ph.D.** (HREB), "A systematic review and meta-analysis of perinatal variables in relation to the risk of testicular cancer."

NIH RECOGNIZES 2010 FARE WINNERS

The NIH Fellows Award for Research Excellence (FARE) Program recognizes achievement in scientific research by intramural postdoctoral fellows and predoctoral fellows currently enrolled in a Ph.D. program and conducting their doctoral dissertation research at NIH. Fellows submit abstracts of their research, which are reviewed by a panel of NIH postdoctoral fellows and principal investigators. Winners receive a $1,000 travel stipend to attend and present their work at a scientific meeting. This year, nine DCEG fellows received such awards.

DCEG Winners: Lisa Mirabello, Tram Lam, Chu-Ling Yu, Joanne Watters, Idan Menashe, Hui-Lee Wong, Scott Quinlan, Sara Schonfeld, and Linda Dong.

DCEG FARE Winners and Abstract Titles

Linda Dong, Ph.D., Occupational and Environmental Epidemiology Branch: *Urinary prostaglandin E2 metabolite and gastric cancer risk in the Shanghai Women's Health Study*

Tram Kim Lam, Ph.D., Genetic Epidemiology Branch: *Dietary quercetin, quercetin-gene interaction, metabolic gene expression in lung tissue, and lung cancer risk*

Idan Menashe, Ph.D., Biostatistics Branch: *Pathway-based analysis of a breast cancer genome-wide association study*

Lisa Mirabello, Ph.D., Clinical Genetics Branch: *Leukocyte telomere length is associated with ovarian cancer in a population-based case-control study*

Scott Quinlan, M.S., Infections and Immunoepidemiology Branch (IIB): *Spectrum of hematologic malignancies associated with solid organ transplantation: Results of a U.S. population-based case-control study*

Sara Schonfeld, M.P.H., Radiation Epidemiology Branch (REB): *Validation of a breast cancer risk assessment tool and its recalibrated version in two large cohorts*

Joanne L. Watters, Ph.D., Nutritional Epidemiology Branch: *Associations between α-tocopherol, β-carotene, and retinol and prostate cancer survival*

Hui-Lee Wong, Ph.D. (IIB): *Systemic cytokine levels and risk of gastric cancer in Chinese women*

Chu-Ling Yu, Sc.D. (REB): *The impact of delayed blood centrifuging, choice of collection tube, and type of assay on 25-hydroxyvitamin D concentrations*

More information about the FARE competition is available at http://felcom.od.nih.gov/subCommittee/fare.aspx. ■

DCEG STAFF WIN NIH PLAIN LANGUAGE AWARDS

Several DCEG staff members were recognized in June at the annual NIH Plain Language Awards ceremony.

Clinical Genetics Branch investigators **Blanche P. Alter, M.D., M.P.H., Neelam Giri, M.D.,** and **Sharon A. Savage, M.D.,** along with Rhonda Wilt DeJoice (NCI Communications Planning and Coordination) and Hong Vo (NIH Office of Research Services), received an award for their publication *Family Research Matters: Inherited Bone Marrow Failure Syndromes Study Newsletter* (http://www.marrowfailure.cancer.gov/IBMFSNewsletter61708.pdf). **Joseph F. Fraumeni, Jr., M.D.,** Division Director, **Samantha Nhan,** Assistant for Special Projects, and **Shelia Hoar Zahm, Sc.D.,** Deputy Division Director, won an award for the Division's newsletter, *Linkage.*

Neelam Giri, Sharon Savage, and Blanche Alter. *(Photograph credit: Alyssa Voss)*

These awards are part of an NIH-wide initiative to promote the use of plain language in all documents written for the public or within the government. Criteria for the award include how clearly the document answers the readers' questions and whether the language is appropriate for the intended audience. Plain language is characterized by the active voice; personal pronouns, such as "we" and "you"; short sentences and paragraphs; and easy-to-understand tables, lists, and other design features.

For more information about the NIH Plain Language Initiative, visit: http://execsec.od.nih.gov/plainlang.

ELEVENTH ANNUAL SUMMER FELLOWS RECOGNITION AND POSTER EVENT

Every summer, DCEG hosts bright and talented students who gain experience conducting research in epidemiology, genetics, statistics, and related fields. Beginning last fall, **Tess Lee,** program assistant in the Office of Education (OE), began fielding inquiries for summer 2009 from interested students. From the more than 300 applications received, 30 summer fellows, ranging from high school to doctoral level, were selected to work with DCEG investigators on cancer research projects.

DCEG summer students and mentors at the Summer Fellows Recognition and Poster Event.

In acknowledgment of the summer fellows' work and an opportunity to present their research projects to DCEG staff, the Division hosted the 11th Annual Summer Fellows Recognition and Poster Event, organized by **Kristin Kiser, M.H.A., M.S.,** fellowship coordinator, OE. The event featured posters by 24 students, who also participated in the NIH Summer Student Poster Session. The afternoon's celebration opened with a recognition ceremony and discussion in which invited 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 OE—shared their perspectives about the future of cancer epidemiology research and scientific career paths.

Students interested in applying for 2010 summer fellowships at DCEG may submit an application to the NIH Summer Internship Program through the NIH Student Programs Web site (www.training.nih.gov/student/index.asp) starting

Posters by 2009 DCEG Summer Fellows

Alex Akman, Washington University in St. Louis
Analysis of linkage disequilibrium across the region defined by a prostate cancer susceptibility marker, rs10896449, and the MYEOV gene in chromosome 11q13
Mentor: **Stephen J. Chanock, M.D.,** Chief of the Laboratory of Translational Genomics (LTG)

Mary Alice Anderson, University of Florida
Black and white differences in breast cancer incidence and the distribution of BMI and reproductive risk factors (1992–2006)
Mentors: **Ruth M. Pfeiffer, Ph.D.,** and **William F. Anderson, M.D., M.P.H.,** both in the Biostatistics Branch (BB)

Bryan Bassig, Yale University, School of Public Health
Selected HLA class II polymorphisms and risk of adult glioma
Mentors: **Alina V. Brenner, M.D., Ph.D.,** and **Ruth A. Kleinerman, M.P.H.,** both in the Radiation Epidemiology Branch (REB)

Rohini Bhatia, University of Rochester
Oral human papillomavirus (HPV) in healthy individuals: A systematic review of the literature
Mentor: **Aimee R. Kreimer, Ph.D.,** Infections and Immunoepidemiology Branch (IIB)

Madeleine Blank, University of Michigan
Dietary fat and risk of ovarian cancer in the NIH-AARP Diet and Health Study
Mentor: **Yikyung Park, Sc.D.,** Nutritional Epidemiology Branch (NEB)

Evan Busch, University of California, Berkeley
The relationship of bacterial translocation to increased incidence of non-Hodgkin lymphoma in HIV+ patients
Mentors: **Anil K. Chaturvedi, Ph.D.,** and **Charles S. Rabkin, M.D.** (both in IIB)

Maria Constanza Camargo, University of Illinois at Chicago
Determinants of Epstein-Barr virus-positive gastric cancer: An international pooled analysis
Mentors: **Charles S. Rabkin, M.D.,** and **Gwen Murphy, Ph.D., M.P.H.** (both in IIB)

Jason Douglas, University of Michigan, School of Public Health
Serum IGF-I, IGF-II, IGFBP-3, and IGF-I/IGFBP-3 molar ratio and risk of pancreatic cancer in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial
Mentor: **Rachael Stolzenberg-Solomon, M.P.H., Ph.D.** (NEB)

Alexander Fischer, University of Maryland, College Park
Urine mutagenicity in the New England Bladder Cancer Study
Mentor: **Dalsu A. N. Baris, M.D., Ph.D.,** Occupational and Environmental Epidemiology Branch

Alison Glassman, University of Kentucky, School of Public Health
Dietary fiber intake and endometrial cancer risk in the NIH-AARP Diet and Health Study
Mentor: **Yikyung Park, Sc.D.** (NEB)

Alpana Kaushiva, University of Maryland, Baltimore County
Correlation between expression of alternative splicing forms of Notch2 *gene and genotypes of genome-wide association studies (GWAS) breast cancer associated SNP rs11249433 in tumors and blood of patients*
Mentor: **Ludmila Prokunina-Olsson, Ph.D.** (LTG)

Katherine McGlynn, Michael Cook, and Catherine Lerro at the NIH Summer Student Poster Session. *(Photograph credit: Alice Sigurdson)*

in mid-November. Students who are specifically interested in cancer epidemiology and genetics are encouraged to learn more about DCEG research and complete a supplemental application at http://dceg.cancer.gov/fellowships/summerprogram. ■

—Kristin Kiser, M.H.A., M.S.

Reflections from 2009 DCEG Summer Fellows

"I had no idea it was possible to have so much fun and learn so much in just a couple of months. Best of all, the people here are even more incredible than the work they are doing: knowledgeable, whip-smart, yet endlessly friendly and helpful." —Evan Busch

"As a returning summer student, I found it an especially rewarding experience to build on the work that I started last summer and to see it progress toward completion." —Alexander Fischer

"My summer at DCEG has not just been about learning the ropes of epidemiology, but also about growing as a researcher. It's been a unique experience where I have learned that interactions with peers and the ability to look critically at research facilitate the transfer of knowledge and the birth of new ideas." —Rohini Bhatia

"The breadth of scientific projects, opportunities to network with distinguished scientists, and the enthusiasm and knowledge of my mentors have contributed to a very enriching research experience at DCEG. My experiences this summer have helped to shape my future research interests and have provided me with a better understanding of the finer points of epidemiologic research." —Bryan Bassig

"Whenever my friends ask me about my summer experience at NCI, I always say I love the research work I have been doing here. My mentor is so great and I have learned a lot from her. My experience at NCI will be a great treasure for my future career." —Min Tang

Peter Kirk, Colby College
Risk of cervical cancer based on HPV infection type
Mentor: **Mark Schiffman, M.D., M.P.H.,** Clinical Genetics Branch (CGB)

Dorothy Kwok, Yale University, School of Public Health
Genetic variation on 8q24 and serum vitamins D and E among Caucasian males
Mentors: **Tamra Meyer, Ph.D.,** and **Ann W. Hsing, Ph.D.,** both in the Hormonal and Reproductive Epidemiology Branch (HREB)

Catherine Lerro, Yale University, School of Public Health
Body size and risk of testicular cancer: A meta analysis
Mentors: **Michael B. Cook, Ph.D.,** and **Katherine A. McGlynn, Ph.D., M.P.H.** (both in HREB)

Luyang Liu, Barnard College, Columbia University
Analysis of fusion transcripts of the JAZF1 *gene associated with susceptibility to prostate cancer*
Mentor: **Ludmila Prokunina-Olsson, Ph.D.** (LTG)

Shannon Lynch, University of Pennsylvania
Mitochondrial DNA copy number and pancreatic cancer risk in the Alpha-Tocopherol, Beta-Carotene Study
Mentor: **Rachael Stolzenberg-Solomon, M.P.H., Ph.D.** (NEB)

Camille Madsen, Brigham Young University
Environmental correlates of classic Kaposi sarcoma in Sicily
Mentor: **James J. Goedert, M.D.** (IIB)

Hazel Nichols, Johns Hopkins Bloomberg, School of Public Health
Contralateral breast cancer in the Surveillance, Epidemiology, and End Results database, 1974–2006
Mentors: **Amy Berrington de Gonzalez, D.Phil.** (REB), and **James V. Lacey, Jr., Ph.D.** (HREB)

Natalia Orduz, University of Maryland, Shady Grove
Allelic expression imbalance in a 3' UTR HLA-DPA1 *single nucleotide polymorphism in human tissues*
Mentor: **Ludmila Prokunina-Olsson, Ph.D.** (LTG)

Anushi Shah, St. Matthews School of Medicine
Study of copy number variation within GWAS-associated region on chr 1p11.2 in DNA from blood of breast cancer patients
Mentor: **Ludmila Prokunina-Olsson, Ph.D.** (LTG)

Douglas Stram, University of California, Berkeley
A prospective analysis of DNA damage and repair capacity and lung cancer risk: A report from the PLCO Cancer Screening Trial
Mentors: **Alice J. Sigurdson, Ph.D.** and **Preetha Rajaraman, Ph.D.** (both in REB)

Min Tang, University of Maryland, College Park
Bone fractures in monoclonal gammopathy of undetermined significance: A population based study
Mentor: **Ruth M. Pfeiffer, Ph.D.** (BB)

Wenting Wang, Florida State University
A Bayesian Cox model for simultaneously evaluating the association between lung cancer survival time and a large number of genetic markers
Mentor: **Kai Yu, Ph.D.** (BB)

Jason Ya, Thomas Jefferson High School
Clinical conditions associated with Th1/Th2 imbalance
Mentor: **James J. Goedert, M.D.** (IIB)

KENNETH CANTOR RETIRES

Kenneth P. Cantor, Ph.D., M.P.H., retired in April from the Occupational and Environmental Epidemiology Branch (OEEB) after a 29-year career at NCI. "Dr. Cantor has contributed enormously to the research and training programs in environmental epidemiology at NCI. Without question, he is the leading authority on cancer associated with pollutants in the drinking water," noted **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director.

Debra Silverman, Kenneth Cantor, and Joseph Fraumeni. *(Photograph credit: Jennifer Loukissas)*

After earning a B.S. in physics from Oberlin College and a Ph.D. in biophysics from the University of California, Berkeley, Dr. Cantor conducted postdoctoral research on the structure of metaphase chromosomes. He subsequently pursued his interests in public health, earning an M.P.H. from the Harvard School of Public Health, where he focused on environmental exposures and related disease. Dr. Cantor then worked in the Health Research Division of the Environmental Protection Agency (EPA). In 1976, he was detailed from EPA to NCI to pursue research in environmental epidemiology, and he officially transferred to NCI in 1980.

Dr. Cantor fostered a collegial work environment, collaborating with investigators worldwide and mentoring numerous young scientists. He substantially increased our understanding of the cancer hazards of occupational exposure to pesticides and of general population exposure to drinking water contaminants, especially disinfection byproducts and arsenic. He was one of the first to detect an association between disinfection byproducts and bladder cancer in an analytic study, and he confirmed this discovery in various geographic locations. He recently showed that genetic markers of susceptibility greatly enhance dose-related risk of bladder cancer after disinfection byproducts exposure, providing a sound mechanistic rationale for the association. He also investigated whether exposure to disinfection byproducts increases the risk for other cancers, such as those of the colon, rectum, and brain.

Dr. Cantor substantially increased our understanding of the cancer hazards of occupational exposure to pesticides and of general population exposure to drinking water contaminants, especially disinfection byproducts and arsenic.

Dr. Cantor's knowledge is apparent in the more than 180 scientific papers he has published. His expertise has been recognized by his service on interagency working groups, committees of the National Academy of Sciences, and monograph working groups at the International Agency for Research on Cancer, as well as by numerous invitations to present his research findings in many venues.

Dr. Cantor will spend his retirement enjoying and expanding his lifelong interest in music. He will continue investigating environmental risk factors for cancer, as well as their interactions with genetic susceptibility, as a part-time advisor to OEEB. ■

—Debra T. Silverman, Sc.D., Sc.M.

DCEG STAFF RECEIVE NIH MERIT AWARDS

At the annual NIH Awards Ceremony in October, the following DCEG staff members received 2009 NIH Merit Awards in recognition of their outstanding achievements:

DCEG Winners: Mark Greene, June Peters, Jackie Lavigne, Rochelle Curtis, Blanche Alter, Neil Caporaso, Maria Teresa Landi, Jennifer Loud, Neelam Giri, Lee Moore, Roni Falk, Philip Rosenberg, Kai Yu, and Sharon Savage. (Not shown: Barry Graubard and Nathaniel Rothman.) *(Photograph credit: Alyssa Voss)*

Neil E. Caporaso, M.D., and **Maria Teresa Landi, M.D., Ph.D.,** both of the Genetic Epidemiology Branch, for designing and conducting the Environment and Genetics in Lung Cancer Etiology study, the most comprehensive etiologic study of lung cancer conducted to date.

Rochelle E. Curtis, M.A., Radiation Epidemiology Branch, for long-standing contributions to NCI's studies to quantify second cancer risks and other serious late effects among cancer and bone marrow transplant patients.

Roni T. Falk, M.S., Hormonal and Reproductive Epidemiology Branch, for enhancing our understanding of the role of endogenous hormones in cancer etiology through methodological work to ensure that measurements are accurate, reproducible, and sensitive.

Inherited Bone Marrow Failure Syndromes Study Team, which includes **Blanche P. Alter, M.D., M.P.H.,** Clinical Genetics Branch (CGB), **Neelam Giri, M.D.** (CGB), **Mark H. Greene, M.D.** (Chief of CGB), **Jennifer T. Loud, R.N., C.R.N.P., D.N.P.** (CGB), **June A. Peters, M.S., C.G.C.** (CGB), **Philip S. Rosenberg, Ph.D.,** Biostatistics Branch (BB), and **Sharon A. Savage, M.D.** (CGB), in collaboration with Ann Carr and Lisa Leathwood from Westat corporation, for creating the world's largest cohort of families with inherited bone marrow failure syndromes and for quantifying the risk of cancer in Fanconi anemia and dyskeratosis congenita.

Jackie Lavigne, Ph.D., M.P.H., Chief of the Office of Education, and **Barry I. Graubard, Ph.D.** (BB), as part of the National Health and Nutrition Examination Survey surplus serum IGF measurement group.

Lee E. Moore, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB), in recognition of her important scientific contributions to furthering our understanding of molecular pathologic factors that play a role in the etiology of urologic cancers.

Nathaniel Rothman, M.D., M.P.H., M.H.S. (OEEB), for important scientific contributions to our understanding of the molecular epidemiology of non-Hodgkin lymphoma.

Sharon A. Savage, M.D. (CGB), for developing DCEG's Genetic Epidemiology of Telomere Maintenance in Cancer Etiology research program and for discovering the TINF2 dyskeratosis congenita susceptibility gene.

Kai Yu, Ph.D. (BB), for developing creative statistical methods for genetic epidemiology with an impact on studies across NCI and the larger scientific community. ■

ALUMNA DR. PETERS SELECTED FOR THE PECASE AWARD

Ulrike Peters

Among 100 recipients, Dr. Ulrike Peters, former postdoctoral fellow in the Nutritional Epidemiology Branch, was selected for the Presidential Early Career Award for Scientists and Engineers (PECASE) by President Obama. The PECASE is the highest honor bestowed by the U.S. government on young professionals in the early stages of their independent research careers.

The award was initiated by President Clinton in 1996. Winners are selected based on two criteria: (1) pursuit of innovative research at the frontiers of science and technology and (2) a commitment to community service, demonstrated through scientific leadership, public education, and community outreach. Winning scientists receive up to a five-year research grant to further their study in support of critical government missions.

Dr. Peters will be recognized at the White House ceremony in the fall. She is currently a research associate professor of epidemiology at Fred Hutchinson Cancer Research Center in Seattle, Washington.

CHARLES LAND RETIRES

Charles E. Land, Ph.D., retired in August from the Radiation Epidemiology Branch (REB) after a 34-year career at NCI. Dr. Land is an internationally acclaimed statistical expert on radiation risk assessment and has carried out pioneering work in modern dose-response analysis and modeling of low-dose cancer risk.

Dr. Land earned a Ph.D. in statistics from the University of Chicago in 1968 and began his career studying radiation at the Atomic Bomb Casualty Commission (ABCC) in Hiroshima, where he conducted the first dose-response analysis of cancer risk in the Life Span Study cohort of atomic bomb survivors in collaboration with the late Dr. Gilbert Beebe. In 1975, Dr. Land joined NCI, where he became a founding member of REB. He continued collaborating with the ABCC and its successor, the Radiation Effects Research Foundation, and led numerous other studies. In a series of seminal investigations, he and his colleagues clarified the pattern of breast cancer risk associated with radiation exposure. These studies provided new mechanistic insights into breast carcinogenesis, while serving as the prototype for epidemiologic studies of other radiogenic cancers.

Dr. Land was instrumental in elucidating the cancer risk following radioactive fallout from the U.S. nuclear weapons tests. In addition, he analyzed data for studies of global and other radioactive fallout scenarios, initiated a study of thyroid nodules among residents in radiation-contaminated Kazakhstan, developed statistical models for radiation-related probability of causation (known as the NIH radioepidemiological tables), and collaborated with other federal agencies to develop an online Interactive RadioEpidemiological Program that incorporated new risk estimates and statistical uncertainty.

Kiyohiko Mabuchi, Elaine Ron, Charles Land, Joseph Fraumeni, and Martha Linet.

In a series of seminal investigations, Dr. Land and his colleagues clarified the pattern of breast cancer risk associated with radiation exposure. These studies provided new mechanistic insights into breast carcinogenesis, while serving as the prototype for epidemiologic studies of other radiogenic cancers.

Dr. Land's numerous awards and honors include the NIH Director's Award, the NCI Charles Harkin Award for Research in Thyroid Cancer, the USPHS Outstanding Service and Meritorious Service medals, and an NIH Merit Award. He has mentored many junior investigators, and he has been a valued advisor across NIH and the federal government as well as to numerous national and international radiation committees. He has been responsible for landmark radiation committee reports on a wide range of issues relating to radiation risk, including lung cancer, genetic susceptibility to cancer, uncertainty in risk estimates, and probability of disease causation, as well as a recent report of the International Commission on Radiological Protection on the extrapolation of radiation-related cancer risk.

To honor his distinguished scientific career, Dr. Land has been selected to present the Thirty-Fourth Lauriston S. Taylor Lecture at the 2010 Annual Meeting of the National Council on Radiation Protection and Measurements.

Dr. Land plans to enjoy his retirement in Portugal, but he will continue to advise DCEG on the complex statistical issues associated with radiation-related cancer. ■

—Ruth A. Kleinerman, M.P.H.,
and Kiyohiko Mabuchi, M.D., Dr.P.H.

SCIENTIFIC HIGHLIGHTS

ALL-CAUSE MORTALITY

Adiposity and Physical Activity

The authors evaluated whether physical activity protects against the adverse effects of high adiposity (assessed by body mass index [BMI] and waist circumference) on all-cause mortality using data on 185,412 men and women in the NIH-AARP Diet and Health Study. During follow-up between 1996 and 2006, overweight (BMI 25 to < 30), obesity (BMI ≥ 30), a large waist circumference (men: ≥ 102 cm; women: ≥ 88 cm), and low physical activity were each independent predictors of mortality. Compared with persons of normal weight (BMI 18.5 to < 25) who were physically active (more than seven hours per week of moderate physical activity), mortality risk ratios were 1.62 for inactive normal-weight persons, 1.79 for active morbidly obese (BMI ≥ 35) persons, and 3.45 for inactive morbidly obese persons. Similar results were found for the combined relation of BMI and vigorous physical activity. Inactive persons with a large waist circumference had two times greater mortality risk than active persons with a normal waist circumference. High physical activity attenuated but did not eliminate the increased mortality risk associated with obesity. **(Koster A, Harris TB, Moore SC, Schatzkin A, Hollenbeck AR, van Eijk JT, Leitzmann MF. Joint associations of adiposity and physical activity with mortality: The National Institutes of Health-AARP Diet and Health Study. *Am J Epidemiol* 2009;169:1344–1351)**

BRAIN CANCER

Lead Exposure and Oxidative Stress Genes

In a hospital-based case-control study, the authors examined modification of the association between occupational lead exposure and brain tumors by single-nucleotide polymorphisms (SNPs) in genes related to oxidative stress. The study included 362 patients with glioma (of which 176 were glioblastoma multiforme [GBM]), 134 patients with meningioma, and 494 controls. When the analyses were restricted to cases with GBM, *RAC2* rs2239774 and two highly correlated *GPX1* polymorphisms (rs1050450 and rs18006688) were found to significantly modify the association with lead exposure after adjusting for multiple comparisons. The same *GPX1* polymorphisms and *XDH* rs7574920 were found to significantly modify the association between cumulative lead exposure and meningioma. Results suggest that lead may cause GBM and meningioma through mechanisms related to oxidative damage. **(Bhatti P, Stewart PA, Hutchinson A, Rothman N, Linet MS, Inskip PD, Rajaraman P. Lead exposure, polymorphisms in genes related to oxidative stress, and risk of adult brain tumors. *Cancer Epidemiol Biomarkers Prev* 2009;18:1841–1848)**

BREAST CANCER

Adding SNPs to a Risk Model

Adding genotypes from seven SNPs that had previously been associated with breast cancer to NCI's Breast Cancer Risk Assessment Tool (BCRAT) increases the area under the receiver operating characteristic curve, a measure of discriminatory accuracy, from 0.607 to 0.632. Criteria based on four clinical or public health applications were used to compare BCRAT with BCRATplus7, a version of the BCRAT tool that includes the seven genotypes. Criteria included number of expected life-threatening events for the decision to take tamoxifen, expected decision losses (in units of the loss from giving a mammogram to a woman without detectable breast cancer) for the decision to have a mammogram, number of lives saved by risk-based allocation of screening mammography, and rates of risk reclassification. Improvements in expected numbers of life-threatening events were 0.07% and 0.81% for deciding whether to take tamoxifen to prevent breast cancer for women aged 50–59 and 40–49 years, respectively. For deciding whether to recommend screening mammograms to women aged 50–54 years, the reduction in expected losses was 0.86% if the ideal breast cancer prevalence threshold for recommending mammography was that of women aged 50–54 years. Improvements from BCRATplus7 were also small for risk-based allocation of mammograms under cost constraints. Cross-classification of risks indicated that some women classified by BCRAT would have different classifications with BCRATplus7, which might be useful if BCRATplus7 was well calibrated. However, models with SNPs, such as BCRATplus7, have not been validated for calibration in independent cohort data. The gains from BCRATplus7 were small in the applications examined. **(Gail MH. Value of adding single-nucleotide polymorphism genotypes to a breast cancer risk model. *J Natl Cancer Inst* 2009;101:959–963)**

Alcohol and Breast Cancer Risk

The authors studied 184,418 postmenopausal women aged 50–71 years in the NIH-AARP Diet and Health Study to investigate the association between alcohol and breast cancer by different tumor characteristics. Alcohol use, diet, and potential risk factors for cancer were assessed with a mailed questionnaire at baseline. Breast cancer cases and estrogen and progesterone receptor status were identified through links to state cancer registries. During an average of seven years of follow-up, 5,461 breast cancer cases were identified. Alcohol

was positively associated with total breast cancer: even a moderate amount of alcohol (> 10 g/day) increased breast cancer risk. In a comparison of > 35 g vs. 0 g/day, the multivariate relative risks (RRs) were 1.35 for total breast cancer, 1.46 for ductal tumors, and 1.52 (95% confidence interval [CI] = 0.95–2.44) for lobular tumors. Compared to 0 g/day, the multivariate RRs for estrogen receptor–positive/progesterone receptor–positive, estrogen receptor–positive/progesterone receptor–negative, and estrogen receptor–negative/progesterone receptor–negative tumors were 1.46 for > 35 g, 1.13 (CI = 0.73–1.77) for > 20 g, and 1.21 (CI = 0.79–1.84) for > 20 g, respectively. Moderate consumption of alcohol was associated with breast cancer, specifically hormone receptor-positive tumors. **(Lew JQ, Freedman ND, Leitzmann MF, Brinton LA, Hoover RN, Hollenbeck AR, Schatzkin A, and Park Y. Alcohol and risk of breast cancer by histologic type and hormone receptor status in postmenopausal women. *Am J Epidemiol* 2009;170:308–317)**

Racial Disparity in Breast Cancer Mortality

Breast cancer mortality rates among black women became higher than those among white women during the late 1980s, and the gap has continued to widen. To further explore the underlying causes of this racial disparity, black-to-white rate ratios (RR_{BW}) for mortality, incidence, hazard of breast cancer death, and incidence-based mortality (IBM) were investigated using data from NCI's Surveillance, Epidemiology, and End Results (SEER) program on 244,786 women diagnosed with breast cancer between 1990 and 2003 and followed through 2004. A counterfactual approach was used to examine the expected IBM RR_{BW}, assuming equal distributions for estrogen receptor (ER) expression, and/or equal hazard rates of breast cancer death among black and white women. From 1990 to 2004, the mortality RR_{BW} was greater than 1.0 and increased over time. In contrast, the incidence RR_{BW} was generally less than 1.0. Absolute hazard rates of breast cancer death declined substantially for ER-positive tumors and modestly for ER-negative tumors but were persistently higher for blacks than for whites. Equalizing the distributions of ER expression in blacks and whites decreased the IBM RR_{BW} slightly. However, when hazard rates of breast cancer death were matched within each ER category, the BW disparity in IBM RR_{BW} was essentially eliminated. Identifying and addressing the reasons for the excess hazards of breast cancer death among black women, especially during the first few years following diagnosis, may help reduce the existing racial disparity in breast cancer mortality rates. **(Menashe I, Anderson WF, Jatoi I, Rosenberg PS. Underlying causes of the black-white racial disparity in breast cancer mortality: A population-based analysis. *J Natl Cancer Inst* 2009;101:993–1000)**

CERVICAL CANCER

Implications of Human Papillomavirus Genotype Distributions

To study how human papillomavirus (HPV) vaccination and HPV-based screening may influence cervical cancer prevention, the authors used the New Mexico SEER registry to ascertain cases of *in situ* (n = 1,213) and invasive (n = 808) cervical cancer diagnosed during 1985–1999 and 1980–1999, respectively. HPV genotyping was performed on tissues from *in situ* and invasive cancers and on cervical Papanicolaou test specimens from control subjects (n = 4,007). The most common HPV genotypes detected in invasive cancers were HPV-16 (53.2%), HPV-18 (13.1%), and HPV-45 (6.1%) and in *in situ* cancers were HPV-16 (56.3%), HPV-31 (12.6%), and HPV-33 (8.0%). Invasive cancer case subjects who were positive for HPV-16 or -18 were diagnosed at younger ages than those who were positive for other carcinogenic HPV genotypes (mean age at diagnosis: 48.1, 45.9, and 52.3 years, respectively). The percentage of subjects with HPV-16–positive *in situ* and invasive cancers, but not of subjects with HPV-18–positive cancers, declined with more recent calendar year of diagnosis, whereas the percentage that were positive for HPV genotypes other than HPV-16 and HPV-18 increased. The subjects' ages at diagnosis of HPV-16– and HPV-18–related invasive cancers were younger than that of subjects with invasive cancers caused by other carcinogenic HPV genotypes, suggesting that the age at initiation of cervical screening could be delayed in HPV-vaccinated populations. **(Wheeler CM, Hunt WC, Joste NE, Key CR, Quint WGV, and Castle PE. Human papillomavirus genotype distributions: Implications for vaccination and cancer screening in the United States. *J Natl Cancer Inst* 2009;101:475–487)**

Loop Electrosurgical Excision Procedure and Subsequent HPV

To examine the impact of treatment for cervical precancerous lesions, the authors compared the acquisition of new HPV infections among HPV-positive women who underwent colposcopy and who were treated by loop electrosurgical excision procedure (LEEP) (n = 195) with those who were untreated (n = 1,625) at entry into a two-year study. Cumulative incidence rate ratios (IRRs) for treated vs. untreated women at 6 and 24 months of follow-up were calculated for infection by individual HPV genotypes, any HPV genotypes, any carcinogenic HPV genotypes, any noncarcinogenic HPV genotypes, and phylogenetic groups of HPV genotypes. Treated women were 29% less likely than untreated women to have carcinogenic HPV genotypes detected at 6-month follow-up (IRR = 0.71) and were 18% less likely to have these genotypes detected at 24-month

follow-up (IRR = 0.82), although neither association was statistically significant. Treated women were 56% less likely to have HPV genotypes of the α9 phylogenetic species, which includes HPV-16, detected at 6-month follow-up (IRR = 0.44) and were 40% less likely to have these genotypes detected at 24-month follow-up (IRR = 0.60). LEEP may reduce the acquisition of certain carcinogenic HPV genotypes related to HPV-16. **(Castle PE, Kreimer AR, Wacholder S, Wheeler CM, Koutsky LA, Rydzak G, Buckman DW, Graubard B, Schiffman M. Influence of loop electrosurgical excision procedure on subsequent acquisition of new human papillomavirus infections. *J Infect Dis* 2009;199:1612–1620)**

GENETICS

Dyskeratosis Congenita

To investigate the spectrum of cancer susceptibility in dyskeratosis congenita (DC), the authors examined more than 500 cases of DC reported in the literature between 1910 and 2008 and conducted a quantitative analysis of cancer risks in 50 patients with DC from NCI's Inherited Bone Marrow Failure Syndrome cohort who had enrolled between 2002 and 2007. Sixty cancers were reported among 52 literature cases, while seven occurred among patients in the NCI DC cohort. The two cohorts were comparable in their median overall survival (age 42 years) and cumulative incidence of cancer (40–50% by age 50 years). The most frequent solid tumors were head and neck squamous cell carcinomas, followed by skin and anorectal cancer. The ratio of observed to expected (O/E) cancers in the NCI cohort was 11-fold compared with the general population. Significantly elevated O/E ratios were 1,154 for tongue cancer and 195 for acute myeloid leukemia. Survival after bone marrow transplantation for aplastic anemia or leukemia was poor in both cohorts. **(Alter BP, Giri N, Savage SA, and Rosenberg PS. Cancer in dyskeratosis congenita. *Blood* 2009;113:6549–6557)**

LYMPHOHEMATOPOIETIC NEOPLASIA

Caspase Genetic Variation and Non-Hodgkin Lymphoma Risk

Caspase genes play a critical role in regulating apoptosis, cell differentiation, inflammation, and innate immunity, and several are mutated or have altered expression in non-Hodgkin lymphoma (NHL). To study the impact of genetic variation in caspases on NHL risk, the authors analyzed tag SNPs in 12 caspase and related genes in three population-based case-control studies (1,946 cases and 1,808 controls). Gene-based analysis, adjusting for the number of tag SNPs genotyped in each gene, showed significant associations for *CASP8, CASP9,* and *CASP1.* SNP-based analysis showed that *CASP8* rs6736233 (odds ratio $[OR]_{CG} = 1.21$, $OR_{CC} = 2.13$); *CASP9* rs4661636 ($OR_{CT} = 0.89$, $OR_{TT} = 0.77$); and *CASP1* rs1785882 ($OR_{AT} = 1.12$, $OR_{AA} = 1.30$) were

MAJOR EDITORIALS, COMMENTARIES, AND REVIEWS PUBLISHED BY DCEG SCIENTISTS IN 2009

Philip E. Castle, Ph.D., Hormonal and Reproductive Epidemiology Branch, et al. "Age-appropriate use of human papillomavirus vaccines in the U.S.," *Gynecol Oncol* 2009;114:365–369

Stephen J. Chanock, M.D., Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics. "High marks for GWAS," *Nat Genet* 2009;41(7):765–766

Eric A. Engels, M.D., M.P.H., Infections and Immunoepidemiology Branch. "Non-AIDS-defining malignancies in HIV-infected persons: Etiologic puzzles, epidemiologic perils, prevention opportunities," *AIDS* 2009;23:875–885

Ethel S. Gilbert, Ph.D., Radiation Epidemiology Branch. "Ionising radiation and cancer risks: What have we learned from epidemiology?" *Int J Radiat Biol* 2009;85:467–482

Patricia Hartge, Sc.D., Epidemiology and Biostatistics Program. "Genetics of reproductive lifespan," *Nat Genet* 2009;41(6):637–638

Donguk Park, Ph.D., Patricia A. Stewart, Ph.D., and **Joseph Coble, Sc.D.,** all of the Occupational and Environmental Epidemiology Branch (OEEB). "A comprehensive review of the literature on exposure to metalworking fluids," *J Occup Environ Hyg* 2009;6:530–541

Anjoeka Pronk, Ph.D., Joseph Coble, Sc.D., and **Patricia A. Stewart, Ph.D.,** all of OEEB. "Occupational exposure to diesel engine exhaust: A literature review," *J Expo Sci Environ Epidemiol* 2009;19:443–457

Sharon A. Savage, M.D., and **Blanche P. Alter, M.D., M.P.H.,** both of the Clinical Genetics Branch. "Dyskeratosis Congenita," *Hematol Oncol Clin North Am* 2009;23:215–231

Arthur Schatzkin, M.D., Dr.P.H., Christian C. Abnet, Ph.D., M.P.H., Amanda J. Cross, Ph.D., all of the Nutritional Epidemiology Branch (NEB); **Ruth M. Pfeiffer, Ph.D., Mitchell H. Gail, M.D., Ph.D.,** both of the Biostatistics Branch; et al. "Mendelian randomization: How it can—and cannot—help confirm causal relations between nutrition and cancer," *Cancer Prev Res* 2009;2:104–113

Arthur Schatzkin, M.D., Dr.P.H., Steven C. Moore, Ph.D., Yikyung Park, Sc.D., all of NEB, et al. "Observational epidemiologic studies of nutrition and cancer: The next generation (with better observation)," *Cancer Epidemiol Biomarkers Prev* 2009;18:1026–1032

significantly associated with NHL risk and associations were consistent across studies. Genetic variants of *CASP8* were associated with risks of all major NHL subtypes. Findings suggest that genetic variation in caspases may play an important role in lymphomagenesis. **(Lan Q, Morton LM, Armstrong B, Hartge P, Menashe I, Zheng T, Purdue MP, Cerhan JR, Zhang Y, Grulich A, Cozen W, Yeager M, Holford TR, Vajdic CM, Davis S, Leaderer B, Kricker A, Schenk M, Zahm SH, Chatterjee N, Chanock SJ, Rothman N, and Wang SS. Genetic variation in caspase genes and risk of non-Hodgkin lymphoma: A pooled analysis of three population-based case-control studies. *Blood* 2009;114:264–267)**

Cell Cycle, Apoptosis, and Lymphocyte Development Regulatory Genes

Because many NHL-associated translocations involve cell cycle, apoptosis, and lymphocyte development regulatory genes, the authors studied NHL risk associated with common genetic variation in 20 candidate genes in these pathways. Genotyping of 203 tag SNPs was conducted in 1,946 NHL cases and 1,808 controls pooled from three independent population-based case-control studies. The most striking associations were observed for tag SNPs in the proapoptotic gene *BCL2L11 (BIM)* and *BCL7A,* which is involved in a rare NHL-associated translocation. Variants in *BCL2L11* were strongly related to follicular lymphoma only, particularly rs3789068 (OR_{AG} = 1.41; OR_{GG} = 1.65). Variants in *BCL7A* were strongly related to diffuse large B cell lymphoma only, particularly rs1880030 (OR_{AG} = 1.34; OR_{AA} = 1.60). The associations for both variants were similar in all three studies and supported by haplotype analyses. Associations for variants in *BCL6, CCND1,* and *MYC* were also observed. Results support the role of common genetic variation in cell cycle, apoptosis, and lymphocyte development regulatory genes in lymphomagenesis and suggest that effects may vary by NHL subtype. **(Morton LM, Purdue MP, Zheng T, Wang SS, Armstrong B, Zhang Y, Menashe I, Chatterjee N, Davis S, Lan Q, Vajdic CM, Severson RK, Holford TR, Kricker A, Cerhan JR, Leaderer B, Grulich A, Yeager M, Cozen W, Zahm SH, Chanock SJ, Rothman N, Hartge P. Risk of non-Hodgkin lymphoma associated with germline variation in genes that regulate the cell cycle, apoptosis, and lymphocyte development. *Cancer Epidemiol Biomarkers Prev* 2009;18:1259–1270)**

Mortality among Formaldehyde Workers

The authors examined associations between quantitative formaldehyde (FA) exposure and death from lymphohematopoietic malignancies for 25,619 workers employed in FA-using or FA-producing plants before 1966 and followed through 2004. They found increased risks for the highest vs. lowest peak FA exposure category (≥ 4 parts per million [ppm] vs. > 0 to < 2.0 ppm) and all lymphohematopoietic malignancies (RR = 1.37). Excess risk was seen for Hodgkin lymphoma (RR = 3.96) and possibly several other subgroups of these malignancies, notably myeloid leukemia, with a 1.78-fold higher risk (CI = 0.87–3.64, p for trend = 0.13). Myeloid leukemia is the type most often associated with chemical exposures. For peak exposure, the highest FA-related risks for myeloid leukemia occurred before 1980, but trend tests did not attain statistical significance until 1990; after the mid-1990s, the FA-related risk of myeloid leukemia declined. Evaluation of risks over time suggests a possible link between FA exposure and lymphohematopoietic malignancies, particularly myeloid leukemia, but also perhaps Hodgkin lymphoma and multiple myeloma. **(Beane Freeman LE, Blair A, Lubin JH, Stewart PA, Hayes RB, Hoover RN, Hauptmann M. Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries: The National Cancer Institute Cohort. *J Natl Cancer Inst* 2009;101:751–761)**

Obesity, Lifestyle Risk Factors, and Myelodysplastic Syndromes

The authors examined the relations of obesity and lifestyle factors to myelodysplastic syndromes (MDS) in a cohort of 471,799 persons aged 50–71 years who were recruited into the NIH-AARP Diet and Health Study during 1995–1996. Incident MDS was diagnosed in 193 persons during 2001–2003. A significant positive association was observed between BMI at baseline and MDS. Compared with persons with a BMI < 25, hazard ratios (HRs) for persons with BMIs of 25 to < 30 and ≥ 30 were 1.15 (CI = 0.81–1.64) and 2.18, respectively. The association was not affected by physical activity, cigarette smoking, or alcohol intake. The risk of MDS was elevated among former smokers (HR = 1.68) and current smokers (HR = 3.17) but not never smokers. Physical activity, alcohol consumption, meat intake, and fruit and vegetable intake did not appear to significantly influence the risk of MDS in this analysis. This prospective investigation of MDS implicates both obesity and smoking as modifiable risk factors. **(Ma X, Lim U, Park Y, Mayne ST, Wang R, Hartge P, Hollenbeck AR, and Schatzkin A. Obesity, lifestyle factors, and risk of myelodysplastic syndromes in a large U.S. cohort. *Am J Epidemiol* 2009;169:1492–1499)**

Occupational Pesticide Exposure and Risk of Monoclonal Gammopathy of Undetermined Significance

The authors assessed the risk of monoclonal gammopathy of undetermined significance (MGUS) among 678 men (aged 30–94 years) from a prospective cohort of pesticide applicators. Age-adjusted prevalence estimates of MGUS were compared with prevalence among 9,469 men from Minnesota. Among 555 study participants older than 50 years of age, 38 (6.8%) were found to have MGUS. Compared with men from Minnesota, the age-adjusted prevalence

of MGUS was 1.9-fold higher among male pesticide applicators. Among applicators, a 5.6-fold, 3.9-fold, and 2.4-fold increased risk of MGUS prevalence was observed among users of the chlorinated insecticide dieldrin, the fumigant mixture carbon-tetrachloride/carbon disulfide, and the fungicide chlorothalonil, respectively. Results support the hypothesis that specific pesticides are causatively linked to myelomagenesis. **(Landgren O, Kyle RA, Hoppin JA, Beane-Freeman LE, Cerhan JR, Katzmann JA, Rajkumar SV, Alavanja MC. Pesticide exposure and risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study. *Blood* 2009;113:6386–6391)**

Polychlorinated Biphenyl and Organochlorine Pesticide Exposures

Carpet dust was used to examine the risk of childhood leukemia in relation to residential exposure to six polychlorinated biphenyl (PCB) congeners and the pesticides α- and γ-chlordane, p,p′-DDT (dichlorodiphenyltrichloroethane), p,p′-DDE (dichlorodiphenyldichloroethylene), methoxychlor, and pentachlorophenol in a California population-based case-control study conducted in 2001–2006 among 184 acute lymphocytic leukemia (ALL) cases aged seven years or younger and 212 matched controls. Detection of any PCB congener in the dust conferred a 2.0-fold increased risk of ALL. Compared with those in the lowest quartile of total PCBs, the highest quartile was associated with a 2.8-fold risk. Significant positive trends in ALL risk were apparent with increasing concentrations of PCB congeners 118, 138, and 153. No positive associations were observed for chlordane, DDT, DDE, methoxychlor, or pentachlorophenol. The associations with PCBs were stronger among non-Hispanic whites than Hispanics despite similar distributions of PCB levels among controls in each racial/ethnic group. Findings suggest that PCBs may represent a previously unrecognized risk factor for childhood leukemia. **(Ward MH, Colt JS, Metayer C, Gunier RB, Lubin J, Crouse V, Nishioka MG, Reynolds P, Buffler PA. Residential exposure to polychlorinated biphenyls and organochlorine pesticides and risk of childhood leukemia. *Environ Health Perspect* 2009;117:1007–1013)**

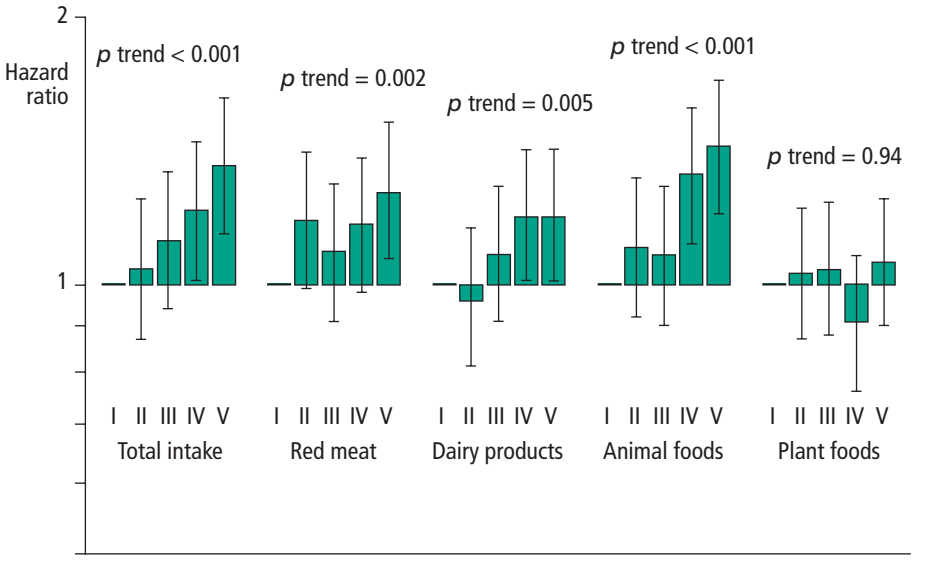


Figure 1. Multivariate-adjusted hazard ratios and 95% confidence intervals for pancreatic cancer risk in association with quintiles of saturated fat intake according to its food sources among 308,736 men and 216,737 women in the NIH-AARP Diet and Health Study. (Thiébaut AC, et al. 2009)

PANCREATIC CANCER

Risks Associated with Alcohol Use

The authors examined the relation between alcohol use and pancreatic cancer risk among 470,681 participants aged 50–71 years during 1995 through 1996 in the NIH-AARP Diet and Health Study, including 1,149 eligible exocrine pancreatic cancer cases identified through 2003. With the referent group being light drinkers (< 1 drink per day), the RRs of developing pancreatic cancer were 1.45 for heavy total alcohol use (≥ 3 drinks per day) and 1.62 for heavy liquor use, compared with the respective referent group. The increased risk with heavy total alcohol use was suggested in never smokers (RR = 1.35; CI = 0.79–2.30) and observed in participants who quit smoking 10 or more years before baseline (RR = 1.41). Findings suggest a moderately increased pancreatic cancer risk with heavy alcohol use, particularly liquor; however, possible residual confounding by cigarette smoking cannot be completely excluded. **(Jiao L, Silverman DT, Schairer C, Thiébaut AC, Hollenbeck AR, Leitzmann MF, Schatzkin A, Stolzenberg-Solomon RZ. Alcohol use and risk of pancreatic cancer: The NIH-AARP Diet and Health Study. *Am J Epidemiol* 2009;169:1043–1051)**

Risks Associated with Dietary Fats

The authors analyzed the association between intakes of fat, fat subtypes, and fat food sources and exocrine pancreatic cancer among 308,736 men and 216,737 women who, as participants in the NIH-AARP Diet and Health Study, had completed a 124-item food frequency questionnaire during 1995–1996. Over an average follow-up of 6.3 years, 865 men and 472 women were diagnosed

with exocrine pancreatic cancer. After conducting multivariable adjustment and combining data for men and women, the authors found that pancreatic cancer risk was directly related to the intakes of total fat (highest vs. lowest quintile; 46.8 vs. 33.2 cases per 100,000 person-years [p-y]; HR = 1.23), saturated fat (51.5 vs. 33.1 cases per 100,000 p-y; HR = 1.36), and monounsaturated fat (46.2 vs. 32.9 cases per 100,000 p-y; HR = 1.22) but not polyunsaturated fat. The associations were strongest for saturated fat from animal food sources (52.0 vs. 32.2 cases per 100,000 p-y; HR = 1.43); specifically, intakes from red meat and dairy products were both significantly associated with increased pancreatic cancer risk (HR = 1.27 and 1.19, respectively) (see Figure 1). In this large prospective cohort with a wide range of intakes, dietary fat of animal origin was associated with increased pancreatic cancer risk. **(Thiébaut AC, Jiao L, Silverman DT, Cross AJ, Thompson FE, Subar AF, Hollenbeck AR, Schatzkin A, Stolzenberg-Solomon RZ. Dietary fatty acids and pancreatic cancer in the NIH-AARP Diet and Health Study. *J Natl Cancer Inst* 2009;101:1001–1011)**

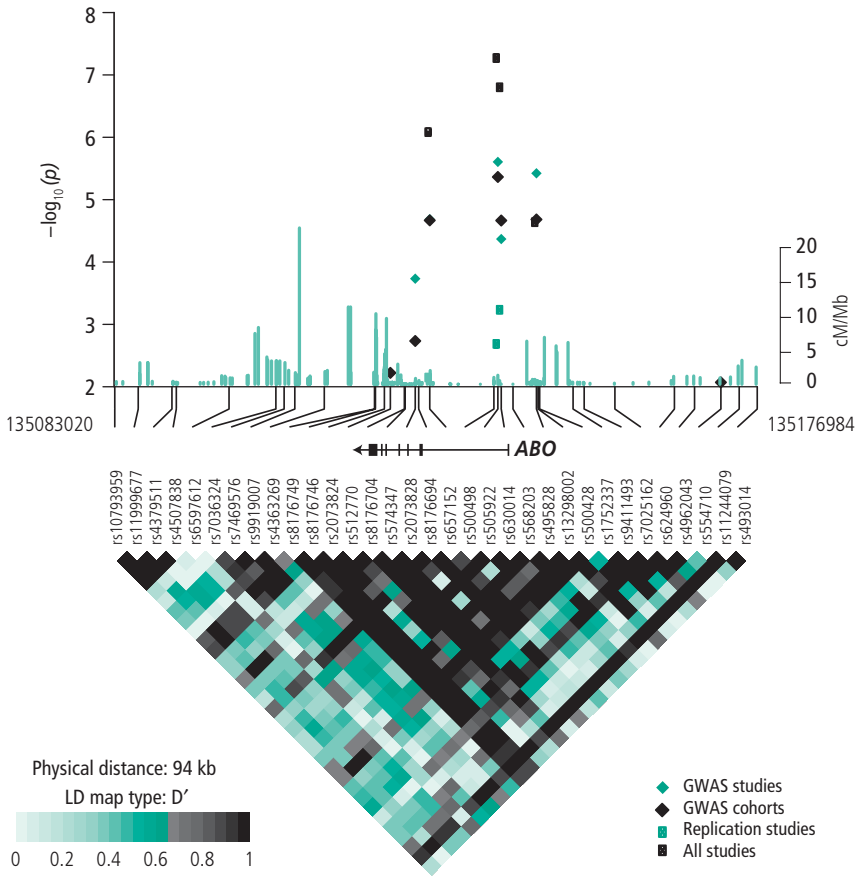


Figure 2. Association and linkage disequilibrium (LD) plot of the 9q34 locus. Association results are shown for all genome-wide association studies (GWAS) (green diamonds), GWAS cohorts (black diamonds), replication studies (green squares), and all studies combined (black squares). (Amundadottir L, et al. 2009)

Variants in *ABO* Locus Related to Risk

The investigators conducted a two-stage genome-wide association study of pancreatic cancer, a cancer with one of the lowest survival rates worldwide. They genotyped 558,542 SNPs in 1,896 individuals with pancreatic cancer and 1,939 controls drawn from 12 prospective cohorts and one hospital-based case-control study. They then performed a combined analysis of these groups, plus an additional 2,457 affected individuals and 2,654 controls from eight case-control studies, adjusting for study, sex, ancestry, and five principal components. The investigators identified an association between a locus on 9q34 and pancreatic cancer marked by the SNP rs505922 (combined $p = 5.37 \times 10^{-8}$; multiplicative per-allele OR = 1.20). This SNP maps to the first intron of the *ABO* blood group gene. Results are consistent with earlier epidemiologic evidence suggesting that people with blood group O may have a lower risk of pancreatic cancer than those with blood group A or B (see Figure 2). **(Amundadottir L, Kraft P, Stolzenberg-Solomon RZ, Fuchs CS, Petersen GM, Arslan AA, Bueno-de-Mesquita HB, Gross M, Helzlsouer K, Jacobs EJ, Lacroix A, Zheng W, Albanes D, Bamlet W, Berg CD, Berrino F, Bingham S, Buring JE, Bracci PM, Canzian F, Clavel-Chapelon F, Clipp S, Cotterchio M, de Andrade M, Duell EJ, Fox Jr JW, Gallinger S, Gaziano JM, Giovannucci EL, Goggins M, González CA, Hallmans G, Hankinson SE, Hassan M, Holly EA, Hunter DJ, Hutchinson A, Jackson R, Jacobs KB, Jenab M, Kaaks R, Klein AP, Kooperberg C, Kurtz RC, Li D, Lynch SM, Mandelson M, McWilliams RR, Mendelsohn JB, Michaud DS, Olson SH, Overvad K, Patel AV, Peeters PH, Rajkovic A, Riboli E, Risch HA, Shu XO, Thomas G, Tobias GS, Trichopoulos D, Van Den Eeden SK, Virtamo J, Wactawski-Wende J, Wolpin BM, Yu H, Yu K, Zeleniuch-Jacquotte A, Chanock SJ, Hartge P, Hoover RN. Genome-wide association study identifies variants in the *ABO* locus associated with susceptibility to pancreatic cancer. *Nat Genet* 2009;41:986–990)**

DCEG PEOPLE IN THE NEWS

In June, **Christian C. Abnet, Ph.D., M.P.H.,** Nutritional Epidemiology Branch (NEB), gave a talk titled "Diet and cancer: Molecular approaches to dietary exposures" at George Washington University in Washington, DC.

Blanche P. Alter, M.D., M.P.H., Clinical Genetics Branch (CGB), delivered invited presentations on inherited bone marrow failure syndromes and cancer risk at meetings in Los Angeles, California, Rotterdam, the Netherlands, and Bern, Switzerland in April and at a June meeting in Adelaide, Australia.

In August, **Dalsu A. N. Baris, M.D., Ph.D., Mark Purdue, Ph.D.,** and **Mary H. Ward, Ph.D.,** all of the Occupational and Environmental Epidemiology Branch (OEEB), gave invited talks at the symposium Organochlorines and Cancer: Recent Findings and Possible Mechanisms at the International Society for Environmental Epidemiology meeting in Dublin, Ireland.

In May, **Porcia T. Bradford, M.D.,** Genetic Epidemiology Branch (GEB), gave two presentations, "Increased risk of second primary cancers after diagnosis of melanoma" and "Cutaneous lymphoma incidence in the United States," at the annual meeting of the Society for Investigative Dermatology in Montreal, Canada.

In August, **Neil E. Caporaso, M.D.** (GEB), cochaired and presented at the Phenotype Harmonization Committee meeting at the NIH-sponsored GENEVA (Gene Environment Association Studies) meeting in Chicago, Illinois.

In May, **Wong-Ho Chow, Ph.D.** (OEEB), gave an invited talk titled "Esophageal adenocarcinoma: Global incidence patterns and clues to etiology" at the International Symposium on Recent Progress on Head and Neck Cancer and Esophageal Cancer organized by the Foundation for Promotion of Cancer Research in Tokyo, Japan.

In July, **Amanda J. Cross, Ph.D.** (NEB), **Mark H. Greene, M.D.,** Chief of CGB, and Hormonal and Reproductive Epidemiology Branch (HREB) members **Philip E. Castle, Ph.D., M.P.H., Jonine D. Figueroa, Ph.D., M.P.H., Ann W. Hsing, Ph.D.,** and **James V. Lacey, Jr., Ph.D.,** gave lectures for the Principles and Practice of Cancer Prevention and Control Course, a part of the NCI Summer Curriculum in Cancer Prevention.

In April, **Leah Ferrucci, Ph.D.** (NEB)—under the mentorship of **Amanda J. Cross, Ph.D.** (NEB), **Barry I. Graubard, Ph.D.,** Biostatistics Branch (BB), **Rashmi Sinha, Ph.D.** (NEB), and Dr. Susan Mayne and Dr. Xiaomei Ma, both of Yale University—successfully defended her doctoral dissertation "The role of meat, meat mutagens, and xenobiotic metabolizing enzymes in neoplasia."

In August, **Mitchell H. Gail, M.D., Ph.D.,** and **Ruth M. Pfeiffer, Ph.D.,** both of BB, taught an invited short course on "Absolute risk projection" at the American Statistical Association in Washington, DC. Dr. Gail also presented "The value of single nucleotide polymophisms (SNPs) in projecting breast cancer risk" at the same meeting and "Applying the Lorenz curve to disease risk to optimize health benefits under cost constraints" at a conference at George Washington University to honor

NIH JURIED ART SHOW

Congratulations to **Annelie M. Landgren, M.P.H.**, Radiation Epidemiology Branch, whose photography piece "Strong Ties" was featured in the 2009 NIH Juried Art Show.

"Strong Ties" by Annelie Landgren.

Ms. Landgren first became interested in photography at the age of 12 and has developed a special interest for symbolism in everyday details. "Strong Ties" was taken in the very early morning at her family's dock in the archipelago northeast of Stockholm, Sweden. The piece represents "strength and support hidden in something seemingly ragged, dirty, and old." This is the first time Ms. Landgren has participated in an art show.

The NIH Juried Art Show celebrates the artistic talent of the NIH community. Forty-three artists were selected from a field of 580 submissions.

Joseph L. Gastwirth. In addition, he gave an invited talk titled "The value of SNPs in projecting breast cancer risk" at the Harvard School of Public Health in September. Dr. Pfeiffer gave an invited lecture about "The probability of detecting disease-associated SNPs in case-control genome-wide association studies" at the National Institute of Environmental Health Sciences' Biostatistics Branch in Research Triangle Park, North Carolina in May.

In May, **Gretchen L. Gierach, Ph.D.,** and **Mark E. Sherman, M.D.,** both of HREB, gave a joint invited presentation on "Opportunities for spectroscopic analysis of breast tissue in epidemiologic studies" to the Biophysics Group of the Optical Technology Division of the National Institute of Standards and Technology in Gaithersburg, Maryland.

Mark H. Greene, M.D., Chief of CGB, presented an educational session titled "Hereditary cancer syndromes: Beyond hereditary breast/ovarian and colorectal cancer" at the American Society for Clinical Oncology meeting in Orlando, Florida and a lecture on "Cancer genomics for gynecologists" at the 2009 Gynecologic Oncology Group semiannual meeting in Baltimore, Maryland.

In June, **Ann W. Hsing, Ph.D.** (HREB), gave an invited talk on "Epidemiology in the 21st century" at the University of Pittsburgh.

In April, **Hormuzd A. Katki, Ph.D.** (BB), gave the alumnus keynote speech "From the magnet to a career in quantitative science" at the 2009 Science, Mathematics, and Computer Science Magnet Research Convention at Montgomery Blair High School in Silver Spring, Maryland.

In May, **Jill Koshiol, Ph.D.,** Infections and Immunoepidemiology Branch, gave an invited presentation titled "Primary human papillomavirus (HPV)-based screening: How to triage HPV positive women with repeat HPV testing" during a Cochrane Workshop on Systematic Reviews on Prevention of Cervical Cancer at the 25th International Papillomavirus Conference in Malmö, Sweden.

Tram Kim Lam, Ph.D. (GEB), received the NCI Cancer Prevention Fellowship program's Merit Award in recognition of her scientific productivity and leadership in the field of cancer prevention and her contributions to and support of the fellowship program.

During June and August, **Huilin Li, Ph.D.** (BB), gave invited talks on "Adjusted maximum likelihood methods in small-area estimation and related problems" at the annual meeting of the International Chinese Statistical Association in San Francisco, California and on "Finding SNP associations with a secondary phenotype in genetic association studies" at the New Researchers in Statistics and Probability Conference in Washington, DC.

In May and June, **Jennifer T. Loud, R.N., C.R.N.P., D.N.P.** (CGB), gave presentations on the role of genetics and genomics in cancer prevention at the NIH Nurse Practitioner Special Interest meeting in Bethesda, Maryland; the inaugural Eastern Tennessee State University Cancer Control and Prevention Conference in Johnson City, Tennessee; and at Georgetown University Graduate School of Nursing & Health Studies in Washington, DC.

In May, **Mary Lou McMaster, M.D.** (GEB), chaired a scientific session and presented a talk on "Precursor disorders in Waldenström macroglobulinemia" at the Third International Patient-Physician Summit on Waldenström Macroglobulinemia in Boston, Massachusetts.

DR. LINET INDUCTED INTO THE JOHNS HOPKINS SOCIETY OF SCHOLARS

Martha S. Linet, M.D., M.P.H., Chief of the Radiation Epidemiology Branch, has been inducted into the Johns Hopkins Society of Scholars in recognition of her seminal scientific contributions and leadership in the epidemiology of leukemia and radiation effects.

Martha Linet

The Society of Scholars consists of former postdoctoral fellows, postdoctoral degree recipients, house staff, and junior or visiting faculty who have served at least one year at Johns Hopkins University but have not been affiliated with the university for at least five years and have thereafter gained marked distinction in the fields of physical, biological, medical, social, or engineering sciences or in the humanities.

In April, **Arthur Schatzkin, M.D., Dr.P.H.,** Chief of NEB, presented "Validation of surrogate endpoints: A cancer perspective" at the Institute of Medicine's workshop Qualification of Biomarkers and Surrogate Endpoints in Chronic Disease in Washington, DC. In June, he co-chaired the Validation Studies of Recovery Biomarkers for Dietary Intake and Physical Activity Session and presented findings from the Observing Protein and Energy Nutrition Study at the International Conference on Diet and Activity Methods in Washington, DC.

At the March International Congress on Occupational Health in South Africa, OEEB led the session Integration of Classic and Molecular Epidemiologic Approaches to Studying Occupational Cancer. OEEB Chief **Debra T. Silverman, Sc.D., Sc.M.,** chaired the session. **Nathaniel Rothman, M.D., M.P.H., M.H.S.,** and Dr. Silverman presented an overview; **Laura Beane Freeman, Ph.D.,** discussed "Occupational formaldehyde exposure and leukemia" and "Classical and molecular cancer epidemiology in the Agricultural Health Study"; **Qing Lan, M.D., Ph.D., M.P.H.,** spoke about "Occupational exposure to trichloroethylene and lymphocyte subset toxicity"; and **Patricia A. Stewart, Ph.D.,** gave a talk titled "Organic solvents and risk of non-Hodgkin lymphoma: Using a module-based approach to exposure assessment in a case-control study."

In June, **Rashmi Sinha, Ph.D.** (NEB), spoke on "Development of dietary intake software for three regions of India" at the International Conference on Diet and Activity Methods in Washington, DC. In July, she spoke on the relationship between meat-related compounds and cancer at Albert Einstein College of Medicine of Yeshiva University in Bronx, New York and at the Mayo Clinic in Rochester, Minnesota.

In April, **Rachael Stolzenberg-Solomon, M.P.H., Ph.D.** (NEB), gave an invited talk titled "Pancreatic cancer: Is there a link with diabetes and insulin resistance?" at the Welch Center for Prevention, Epidemiology, and Clinical Research Grand Rounds at the Johns Hopkins Medical Institutions in Baltimore, Maryland.

In May, **Rose Yang, Ph.D., M.P.H.** (GEB), spoke on "Germ-line copy number variations in melanoma-prone families without known mutations" at the World Congress on Melanoma and at the Congress of the European Association of Dermato-Oncology in Vienna, Austria.

In May, **Regina G. Ziegler, Ph.D., M.P.H.,** Epidemiology and Biostatistics Program, gave an invited presentation on "A new approach to measuring steroid hormone exposure and metabolism in epidemiologic studies" at the International Steroid Analytics Meeting in Munich, Germany.

ADMINISTRATIVE RESOURCE CENTER UPDATES

Joan Starr and Roberto Minutillo.

Roberto P. Minutillo was promoted in January to Deputy Manager of the Administrative Resource Center (ARC). In this capacity, he oversees procurement, manages space and facilities, and supervises several senior administrative officers (AOs) who provide services to DCEG branches. Mr. Minutillo received a B.S. degree in legal studies from the University of Maryland in 1990 and began working at NIH in 1991 as a purchasing agent in the NCI Clinical ARC in Building 10. From 1996 to 1999, he participated in the NCI Administrative Career Development Internship Program, where he gained additional administrative experience through rotations with the NCI Executive Officer, the NCI Office of Grants Administration, the NCI Office of Acquisitions, and the NCI Office of Management. Upon completing the program, he accepted an AO position in DCEG's ARC. In 2006, he transferred to the National Institute of Arthritis and Musculoskeletal and Skin Diseases but returned to NCI in 2007 as the DCEG ARC's lead AO. With his extensive administrative experience, professional commitment, and know-how, Mr. Minutillo will be an asset to DCEG in his new position as Deputy ARC Manager.

Joan Starr has joined DCEG as the lead AO for the ARC. In this role she will provide administrative services for the Laboratory of Translational Genomics and the Core Genotyping Facility and will coordinate special projects for both the ARC and the Division. She previously worked in the NCI Office of the Director ARC in Building 31, as an AO at the National Institute on Aging, and in various administrative roles at the National Institute of Biomedical Imaging and Bioengineering and at the National Institute of Diabetes and Digestive and Kidney Diseases. Ms. Starr brings to the ARC years of professional experience at NIH, excellent customer service and problem-solving skills, and a fresh perspective.

—Donna Siegle

COMINGS . . . GOINGS

Jiyoung Ahn, Ph.D., left the Nutritional Epidemiology Branch (NEB) to take an assistant professor position in the Division of Epidemiology in the Department of Environmental Medicine at New York University School of Medicine.


Cindy Chang

Cindy M. Chang, Ph.D., joined the Infections and Immunoepidemiology Branch (IIB) as a postdoctoral fellow. She received a Ph.D. in epidemiology from the University of North Carolina at Chapel Hill, where she examined risk factors for non-Hodgkin lymphoma molecular subtypes defined by common translocations. Under the mentorship of **Allan Hildesheim, Ph.D.,** she will work on multiple projects involving malignances associated with hematopoiesis and the Epstein-Barr virus.

An industrial hygienist with the Occupational and Environmental Epidemiology Branch (OEEB) since 1999, **Joseph Coble, Sc.D.,** moved to the U.S. Department of Agriculture, where he will work on reducing health hazards associated with the meat industry.

A senior investigator from INSERM at the Institut Gustave Roussy, **Florent de Vathaire, Ph.D.,** joined the Radiation Epidemiology Branch (REB) as a special volunteer for a six-month sabbatical. He will work with **Alice J. Sigurdson, Ph.D.,** and **Alina V. Brenner, M.D., Ph.D.,** on studies of thyroid cancer and brain tumors.


Alexandra Ekblom

Alexandra Ekblom, M.P.H., joined the Office of Communications and Special Initiatives as an NCI Health Communications Intern. She received an M.P.H. from the George Washington University's School of Public Health and Health Services, where she focused on maternal and child health. Previously, she worked on the Employee Wellness Initiative at the National Heart, Lung, and Blood Institute, volunteered at MetroTeen AIDS, and worked as a paralegal. During her six-month internship, she will work with **Jennifer K. Loukissas, M.P.P.,** on numerous communications initiatives.

Leah Ferrucci, Ph.D., left NEB for a postdoctoral fellowship at Yale University's School of Nursing.


Joseph Fraumeni presents a DCEG Special Appreciation Award to Michael Brown.

Michael Brown left the DCEG Administrative Resource Center (ARC) in July to accept a promotion to supervisory purchasing agent at the National Eye Institute. He began his career with the ARC as a purchasing agent in 1999.


Melissa Friesen

Melissa Friesen, Ph.D., joined OEEB as a tenure-track investigator. She received a Ph.D. from the School of Occupational and Environmental Hygiene at the University of British Columbia in Vancouver, where she worked on strategies to minimize misclassification in epidemiologic studies of wood dust, fungicide, and noise exposures in sawmill workers and polycyclic aromatic hydrocarbon exposures in aluminum smelter workers. As a postdoctoral fellow, she continued her research on quantitative exposure assessment strategies at Monash University in Melbourne, Australia and at the University of California, Berkeley.

Meg R. Gerstenblith, M.D., returned to the Genetic Epidemiology Branch (GEB) as a CRTA fellow after a three-year absence. Working with **Alisa M. Goldstein, Ph.D.,** Dr. Gerstenblith will pursue her research interest in skin cancer, focusing particularly on melanoma. Dr. Gerstenblith received her medical degree from Johns Hopkins University School of Medicine in 2004 and came to GEB as a postdoctoral fellow in 2005. In 2006, she left to complete her residency in dermatology at Johns Hopkins University Hospital. During her last year there, she was chief resident in dermatology.


Asieh Golozar

Asieh Golozar, M.D., M.P.H., joined GEB as a visiting fellow. She received a medical degree from Tehran University of Medical Sciences in 2005 and an M.P.H. from Tehran University

in 2007. Since 2005, she has worked as a research fellow on the Gastric and Esophageal Malignancies in Northern Iran project, a collaboration of scientists from Iran, the International Agency for Research on Cancer, and DCEG. In 2008, she completed her first year as a doctoral student in genetic epidemiology at the Johns Hopkins Bloomberg School of Public Health. Dr. Golozar is working with **Alisa M. Goldstein, Ph.D.,** and **Philip R. Taylor, M.D., Sc.D.,** to conduct studies of genetic susceptibility and upper gastrointestinal cancer.


Summer Han

Summer Seongmin Han, Ph.D., joined the Biostatistics Branch (BB) as a research fellow. She received a Ph.D. from the Department of Statistics at Yale University in 2009 and has a master's degree in both statistics and economics. Her doctoral dissertation was on the use of likelihood ratio tests in variance component models for identifying genetic risk factors for complex disorders. Dr. Han will work with **Philip S. Rosenberg, Ph.D.,** and **Nilanjan Chatterjee, Ph.D.,** on methodological research and genetic epidemiology studies.


Jonathan Hofmann

Jonathan Hofmann, Ph.D., joined OEEB as a postdoctoral fellow. He received a Ph.D. in 2008 from the Department of Epidemiology at the University of Washington, where he worked with the Pacific Northwest Agricultural Safety and Health Center on various projects related to farm worker health and safety. For his dissertation, he investigated occupational and genetic determinants of serum cholinesterase inhibition among organophosphate-exposed agricultural pesticide handlers.

He will work with **Mark Purdue, Ph.D.,** on occupational and molecular epidemiologic investigations of kidney cancer and with **Michael C. R. Alavanja, Dr.P.H.,** and **Laura Beane Freeman, Ph.D.,** on the Agricultural Health Study.

Li Jiao, M.D., Ph.D., left NEB to take an assistant professor position at Baylor College of Medicine in Houston.

Farin Kamangar, M.D., Ph.D., left NEB to serve as the chair of the Department of Public Health Analysis at Morgan State University in Baltimore.

Larissa Korde, M.D., M.P.H., left the Clinical Genetics Branch (CGB) to take an assistant professor position in the Division of Oncology at Fred Hutchinson Cancer Research Center in Seattle, Washington.

James V. Lacey, Jr., Ph.D., of the Hormonal and Reproductive Epidemiology Branch (HREB), and **Sophia S. Wang, Ph.D.,** of the Infections and Immunoepidemiology Branch, have each accepted positions as associate professors at the City of Hope, an NCI-designated Comprehensive Cancer Center in Duarte, California.

Dr. Lacey joined HREB as a fellow in 1998 after receiving a doctorate in epidemiologic science from the University of Michigan School of Public Health. He became a tenure-track investigator in 2001. While in HREB, he published seminal articles on the risks of ovarian and endometrial cancers among women who received menopausal hormone therapy. He was also principal investigator for a study of progression from endometrial hyperplasia to carcinoma, the Breast and Bone Follow-up of the FIT Study, and a new cohort including breast and colorectal cancer incidence based in the Kaiser Permanente Northwest and Northern California health plans.

Dr. Wang joined DCEG as a tenure-track investigator in 2000 after receiving a doctorate in epidemiology from the Johns Hopkins Bloomberg School of Public Health and serving as an Epidemic Intelligence Service officer at the Centers for Disease Control and Prevention. She has published extensively on host susceptibility to non-Hodgkin lymphoma (NHL); was co-principal investigator for the genetic component of the NCI/Surveillance, Epidemiology, and End Results multi-center NHL case-control study; was principal investigator for an NIH Bench-to-Bedside Award project to evaluate the role of genetic variation in NHL survival; and received a DCEG Outstanding Mentoring Award. She has also led the SUCCEED (Study to Understand Cervical Cancer Early Endpoints and Determinants), a unique DCEG resource of frozen cervical tissue samples spanning the disease spectrum (i.e., normal to cancer), and the Genetic Supplementation Study, within the Guanacaste Natural History Study, to evaluate the role of genetic variation in human papillomavirus persistence and progression to cervical cancer.

Drs. Lacey and Wang will be missed, but they will continue to collaborate with DCEG on these important research projects.

—Patricia Madigan


James Lacey and Sophia Wang say goodbye to DCEG.


Christian Kratz

Christian Kratz, M.D., joined CGB as a tenure-track investigator. He is board-certified in pediatrics and pediatric hematology/oncology and previously worked on the academic faculty at the University of Freiburg in Germany. He has conducted genetic research studies on childhood myelodysplastic syndromes, myeloproliferative disorders, and childhood cancer predisposition syndromes. Through his research, he has identified germline mutations in the *KRAS* gene as a cause of two related developmental disorders, Noonan syndrome and cardio-facio-cutaneous syndrome. In 2008, he became clinical chair of the Department of Pediatric Oncology in New Zealand's capital, Wellington. In CGB, he will study familial testicular cancer, Shwachman-Diamond syndrome, and Diamond-Blackfan anemia families as well as other familial cancer syndromes of childhood.


Victoria Landsman

Victoria Landsman, Ph.D., joined BB as a postdoctoral fellow. She has a Ph.D. in statistics from the Hebrew University in Israel, where she developed methods for estimating treatment effects from observational data. She will work with **Barry I. Graubard, Ph.D.,** and other BB scientists to identify causal relationships in complex genetic and environmental data collected in epidemiologic studies and to develop skills and experience in the biostatistical methods used in population genetics, molecular epidemiology, and environmental epidemiology.

Rayna Matsuno Weise, M.S., M.P.H., left BB to take a position as a research epidemiologist at the Cancer Research Center of Hawaii.


Alison Mondul

Alison Mondul, Ph.D., joined NEB as a postdoctoral fellow. She received a Ph.D. in cancer epidemiology from the Johns Hopkins Bloomberg School of Public Health, where she studied the relationship between statin use, cholesterol, and prostate cancer with her mentor, Dr. Elizabeth Platz. Prior to her doctoral work at Johns Hopkins, Dr. Mondul earned an M.S.P.H. in epidemiology from Emory University and worked at the American Cancer Society in Atlanta, Georgia. She will work with **Demetrius Albanes, M.D.,** on risk factors for prostate cancer.


Megan Murphy

Megan Murphy, M.S., joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a predoctoral fellow. She has a B.Eng. in chemical engineering from McGill University and an M.S. in biostatistics from Columbia University. She is working with **Nicolas Wentzensen, M.D., Ph.D.,** and other DCEG researchers on the molecular epidemiology of ovarian cancer and other gynecologic malignancies.


Gila Neta

Gila Neta, Ph.D., joined REB as a postdoctoral fellow. She received a Ph.D. from the Johns Hopkins Bloomberg School of Public Health in June. She will work on the genetic risk of thyroid cancer with **Alice J. Sigurdson, Ph.D.,** and on a genetic study of brain tumors with **Preetha Rajaraman, Ph.D.**

David Ng, M.D., left GEB to join the Genetic Disease Research Branch of the National Human Genome Research Institute.

Colleen Pelser, Ph.D., left IIB for a postdoctoral fellowship in the Department of Epidemiology and Preventive Medicine at the University of Maryland School of Medicine in Baltimore.

Carolina Porras, Ph.D., joined IIB as an ORISE postdoctoral fellow. She is a co-investigator on the Costa Rican Human Papillomavirus (HPV) Vaccine Trial. Trained in microbiology, she is affiliated with the Proyecto Epidemiológico Guanacaste in Costa Rica. She will spend one year at IIB working with **Allan Hildesheim, Ph.D.,** and the HPV Vaccine Trial group.

Jian-Song Ren, Ph.D., left NEB to work as a postdoctoral fellow at the International Research Agency on Cancer in Lyon, France.

Ritsu Sakata, Ph.D., left REB and returned to the Radiation Research Foundation in Japan.


Joshua Sampson

Joshua Sampson, Ph.D., joined BB as a tenure-track investigator. He received his Ph.D. in 2007 from the Department of Biostatistics at the University of Washington. For his dissertation, he developed statistical methodology for "genetical genomics," finding improved methods for mapping genetic loci for quantitative gene expressions. After graduation, he continued his work in statistical genetics as a postdoctoral fellow with Dr. Hongyu Zhao at Yale University's Center for Statistical Genomics and Proteomics, where he focused on finding disease-causing quantitative trait loci in genome-wide association studies and identifying ancestry informative markers.

Gillermo Seratti, M.D., left CGB and returned to a medical practice in Argentina.


Fatma Shebl

Fatma Shebl, M.D., Ph.D., joined IIB as a research fellow. Under the mentorship of **Allan Hildesheim, Ph.D.,** she received a Ph.D. in epidemiology from the University of Maryland, Baltimore, where she developed methods for adjusting misclassification errors of incidence estimates. Her current research involves using linked databases to evaluate cancer risk among people with such diseases as end-stage renal disease, hepatitis C virus, and AIDS. In addition, she is studying risk factors for biliary tract cancer, patterns of immune response to HPV-16/18 vaccine, and the genetics of hepatitis C virus clearance.


Jianxin Shi

Jianxin Shi, Ph.D., joined BB as a tenure-track investigator. He received a Ph.D. in statistics from Stanford University in 2006. He conducted postdoctoral research at Stanford University School of Medicine in the Department of Psychiatry and Behavior Sciences and the Department of Health Research and Policy, where he later was appointed as a research scientist. His research interests include statistical problems arising from mapping complex diseases and quantitative traits based on both families and unrelated subjects. His current research projects include detecting disease-associated copy number variants, combining genotype data and expression data, meta-analysis, and developing methods for predicting functional genetic variants.


Rebecca Smith-Bindman

Rebecca Smith-Bindman, M.D., a professor of radiology and biomedical imaging; epidemiology and biostatistics; and obstetrics, gynecology, and reproduction sciences at the University of California, San Francisco, has joined REB for a 10-month sabbatical. Her research focuses on evaluating population patterns of diagnostic testing and the relative risks, benefits, and outcomes associated with imaging. At REB, she will work with **Amy Berrington de Gonzalez, D.Phil., Choonsik Lee, Ph.D.,** and other Division researchers on large population data sets to assess population exposures to diagnostic tests, models for accurately estimating radiation exposure from these tests, and observational studies to assess the association between high exposure and cancer risk.


Min Tang

After three months as a summer student, **Min Tang, M.S.,** joined BB as a predoctoral fellow. She is working on her doctorate in mathematical statistics with Dr. Eric Slud at the University of Maryland and with **Ruth M. Pfeiffer, Ph.D.** Ms. Tang's thesis involves assessing goodness of fit for generalized linear mixed models that can be applied to correlated data in epidemiologic studies.

Lauren Wilson, Sc.M., joined HREB as a predoctoral fellow. She has a master of science in epidemiology from


Lauren Wilson

the Johns Hopkins Bloomberg School of Public Health and is pursuing her doctoral degree there under the mentorship of Dr. Patti Gravitt. Ms. Wilson will work with **Philip E. Castle, Ph.D., M.P.H.,** on visual, microscopic, and molecular measures of cervical inflammation and their relationship to the natural history of HPV.

Hui-Lee Wong, Ph.D., left IIB to join the U.S. Food and Drug Administration.

Visiting scientists **Songnian Yin, Ph.D.,** and **Guilian Li, Ph.D.,** left OEEB and returned to the Institute of Occupational Health and Poison Control at the Chinese Centers for Disease Control after working on a collaborative study of carcinogenicity related to occupational benzene exposure.


Fei Yue

Fei Yue, M.D., a toxicologist from the Guangdong Poisoning Control Center in China, joined OEEB as a visiting scientist for one year. His major research area is the relationship between occupational exposure to trichloroethylene and risk of cancer and other diseases.

HIGHLY CITED PAPERS BY DCEG

Cancer Epidemiology, Biomarkers, and Prevention recently announced the 20 most cited papers published in the journal during 2007, and 3 of them were from DCEG: "Differences in risk factors for breast cancer molecular subtypes in a population-based study" (Yang XR, Sherman ME, Rimm DL, Lissowska J, Brinton LA, Peplonska B, Hewitt SM, Anderson WF, Szeszenia-Dabrowska N, Bardin-Mikolajczak A, Zatonski W, Cartun R, Mandich D, Rymkiewicz G, Ligaj M, Lukaszek S, Kordek R, García-Closas M); "Serum lycopene, other carotenoids, and prostate cancer risk: A nested case-control study in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial" (Peters U, Leitzmann MF, Chatterjee N, Wang Y, Albanes D, Gelmann EP, Friesen MD, Riboli E, Hayes RB); and "Reproducibility of serum sex steroid assays in men by RIA and mass spectrometry" (Hsing AW, Stanczyk FZ, Belanger A, Schroeder P, Chang L, Falk RT, Fears TR).

DCEG PARTICIPATES IN THE AMERICAN COLLEGE OF EPIDEMIOLOGY MEETING

The American College of Epidemiology held its annual meeting in Silver Spring, Maryland in September, with a focus on Novel Methods at the Intersection of Epidemiology and Policy Making. Several members of DCEG received awards, chaired symposia, or presented posters on current research.

Louise A. Brinton, Ph.D., Chief of the Hormonal and Reproductive Epidemiology Branch, received the prestigious Abraham Lilienfeld Award for her exceptionally productive career in cancer epidemiology. Upon receiving the award, she gave the Lilienfeld Award Lecture, reflecting on the uniqueness of epidemiology as a science and the ways in which the discipline has evolved. She emphasized the critical importance of training the next generation of epidemiologists and knowing how to conduct field work.

Leah Ferrucci, Ph.D., Nutritional Epidemiology Branch, won the 2009 Student Prize for her paper "Dietary meat intake in relation to colorectal adenoma in asymptomatic women" and gave a plenary presentation on the results of her research. **Mark Schiffman M.D., M.P.H.,** Clinical Genetics Branch, along with Dr. Deborah Winn, Deputy Director of the Division of Cancer Control and Population Sciences, moderated an expert panel on human papillomavirus (HPV) titled "Epidemiology research needs on HPV and cervical neoplasia, with a special focus on the impact of HPV vaccination on screening recommendations," and **Hormuzd A. Katki, Ph.D.,** Biostatistics Branch, spoke about "Risk estimation for the next generation of cervical cancer prevention programs" during the panel. **Patricia Hartge, Sc.D.,** Epidemiology and Biostatistics Program, chaired the symposium Translating Epidemiology to Policy. **Kathryn Hughes, M.P.H.,** Occupational and Environmental Epidemiology Branch (OEEB), presented her poster "Cancer incidence among pesticide applicators exposed to methyl bromide in the Agricultural Health Study"; **Briseis Kilfoy, Ph.D.** (OEEB), presented her poster "Thyroid cancer and exposure

Louise Brinton gives the Lilienfeld Award Lecture.

to dietary nitrate and nitrite in the NIH-AARP Diet and Health Study"; and **Chu-Ling Yu, Sc.D.,** Radiation Epidemiology Branch (REB), presented her poster "The impact of delayed blood centrifuging, choice of collection tube, and type of assay on 25-hydroxyvitamin D concentrations." **Jackie Lavigne, Ph.D., M.P.H.,** Chief of the Office of Education (OE), and **Martha S. Linet, M.D., M.P.H.,** Chief of REB, presented the mentoring workshop, and **Kristen Kiser, M.H.A., M.S.** (OE), managed the DCEG exhibit and recruitment booth. ■

—Alexandra Ekblom, M.P.H.

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