

Linkage

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Public Policy Impact of Occupational and Environmental Epidemiology

At the December meeting of NCI's National Cancer Advisory Board (NCAB), three DCEG investigators presented recent findings demonstrating the impact that occupational and environmental epidemiology has on public policy. **Joseph F. Fraumeni, Jr., M.D.**, Division Director, began the report with an overview of the Division's occupational and environmental research portfolio. He explained that epidemiology allows researchers to discover carcinogens that are difficult to find using experimental approaches. Of particular importance are studies of workplace exposures, which are usually greater, more frequent, and longer in duration than exposures in the general population. Occupational studies allow researchers to discover mechanisms of carcinogenicity by integrating epidemiology, toxicology, and genetics. Noting that such studies have uncovered many established or probable human carcinogens, Dr. Fraumeni described some of the benefits of the studies: occupational groups can act as sentinels for risks from lower-level exposures in the general population, and the occupational setting affords special opportunities for primary prevention. Some of the DCEG studies have been conducted in high-incidence areas detected by the U.S. cancer mortality atlases published by DCEG scientists. These and other studies have informed public policy measures, including the setting of environmental regulations.

To illustrate the role of epidemiology in public policy, **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, Occupational and Environmental Epidemiology Branch (OEEB), spoke on "Benzene exposure and risk of leukemia and lymphoma." For more than 20 years, DCEG investigators have collaborated with the Chinese



NCAB Presenters: Joseph Fraumeni, Qing Lan, Laura Beane Freeman, and Nathaniel Rothman with OEEB Chief Debra Silverman (center).

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Center for Disease Control and Prevention on studies of occupational exposure to benzene that have greatly increased our understanding of the carcinogenic risks of benzene and helped set standards for benzene exposure in the United States and abroad. In the largest cohort study to establish a link between benzene exposure and acute non-lymphocytic leukemia (ANLL) and myelodysplastic syndrome, the group reported in 1997 that increased risk of ANLL and myelodysplastic syndrome was present at exposures lower than 10 parts per million. Benzene was also linked to other forms of leukemia and to suggestive excesses of non-Hodgkin lymphoma (NHL) and lung cancer. Researchers followed up on these findings by conducting molecular epidemiology studies that used a panel of biomarkers to identify the underlying mechanisms of benzene-related leukemia, including precursor conditions and susceptibility states. Hematologic toxicity was found to occur at lower levels of benzene exposure than generally appreciated, inspiring a larger study that uncovered hematotoxicity among workers exposed to less than 1 part per million in the air, the current U.S. occupational standard. Further analyses identified several genetic variants associated with a decrease in white blood cell counts among exposed workers.

The findings from these studies led to a lower occupational standard in China and greatly informed the risk assessment process for environmental exposures in the United States. In addition, they helped prompt the U.S. Environmental Protection Agency (EPA) to establish a rule limiting the benzene content in gasoline and to adopt controls on passenger vehicles and portable fuel containers to reduce the emission of hazardous air pollutants. In October 2009, the International Agency for Research on Cancer (IARC) used the NCI and other data to conclude that, in addition to ANLL,

there is limited evidence that benzene causes acute and chronic lymphocytic leukemia, NHL, and multiple myeloma. “The decision by the IARC working group provides support for the hypothesis that benzene may be associated with one or more subtypes of lymphoma, a finding that is currently being followed up by DCEG investigators and other research groups,” Dr. Rothman noted. Investigators in OEEB and the Radiation Epidemiology Branch (REB), along with **Martha S. Linet, M.D., M.P.H.**, Chief of REB, are pursuing the cancer risks of different levels of benzene exposure and searching for carcinogenic mechanisms, including markers of genetic susceptibility. DCEG investigators also are collaborating with **Stephen J. Chanock, M.D.**, Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, on a genome-wide scan of benzene-induced hematotoxicity.

In the next presentation, **Laura Beane Freeman, Ph.D.** (OEEB), spoke on “Formaldehyde exposure and the risk of nasopharyngeal cancer and leukemia.” In 1995, the Occupational Safety and Health Administration estimated that 2.1 million U.S. workers were exposed to formaldehyde. A substantially larger number in the general population are exposed to lower levels of formaldehyde through pressed-wood products, glues and adhesives, paper product coatings, insulation materials, cigarette smoke, automobile emissions, and unvented fuel-burning appliances. In the early 1980s, **Aaron E. Blair, Ph.D., M.P.H.**, scientist emeritus of OEEB, established a cohort of workers in formaldehyde-producing and formaldehyde-using plants. Investigators found an increased risk of nasopharyngeal cancer and a possible excess of lymphohematopoietic malignancies. In the most recent analysis of lymphohematopoietic malignancies, which included follow-up through 2004, Dr. Beane Freeman found that the excess

risk was most pronounced for myeloid leukemia. In addition, DCEG studies of professional groups exposed to formaldehyde, such as pathologists, anatomists, and embalmers, showed excess mortality from lymphohematopoietic malignancies, particularly leukemia. To follow up on these findings, DCEG scientists updated a study of funeral industry workers that revealed a three-fold increased risk of myeloid leukemia associated with longest duration of embalming, greatest number of embalmings performed, and highest cumulative exposure to formaldehyde.

To investigate the biological plausibility of leukemia-associated risks from formaldehyde exposure, NCI investigators turned to the multidisciplinary research approach used in the benzene studies. They teamed with colleagues at the Guangdong Poison Control Center and the University of California, Berkeley, to conduct a cross-sectional molecular epidemiology study of Chinese workers exposed to formaldehyde. The results showed significantly lowered peripheral blood cell counts among formaldehyde-exposed workers and leukemia-specific chromosome changes in myeloid progenitor cells.

Dr. Beane Freeman emphasized that “epidemiologic studies combined with emerging molecular technologies are essential in addressing important scientific questions, the answers to which have implications for protecting the public’s health” and described the risk assessment process that has taken place in the evaluation of formaldehyde. In 2004, IARC classified formaldehyde as a human carcinogen because of its association with nasopharyngeal cancer in humans and nasal cancer in rodents and found strong but not sufficient evidence for leukemia. In 2009, using additional epidemiological and mechanistic evidence provided by NCI and

other groups, an IARC working group determined that sufficient evidence was found to link formaldehyde to leukemia, particularly myeloid leukemia. Also in 2009, the National Toxicology Program convened an outside expert panel for its Report on Carcinogens that cited sufficient evidence for leukemia as well as nasopharyngeal and sinonasal cancers. The EPA is updating its risk assessment of formaldehyde, which will be used to determine regulatory standards.

Qing Lan, M.D., Ph.D., M.P.H. (OEEB), concluded the NCAB session with a talk on “Indoor air pollution from coal combustion and risk of lung cancer.” For more than a decade, DCEG researchers have collaborated with Chinese scientists on studies of indoor air pollution from solid fuel use in Xuanwei County, China. This type of pollution is the eighth largest risk factor for global disease. Half of the world’s population is exposed to smoke from cooking or heating with solid fuels, and the greatest exposures occur in developing countries.

“The Xuanwei region provides a unique opportunity to study lung cancer associated with environmental pollution,” Dr. Lan said. “It has the highest prevalence of lung cancer in China, and the attributable risk of lung cancer from unvented smoky coal burning is greater than 90 percent. Also, the lung cancer mortality rates for men and women are similar, yet nearly all women and few men cook, whereas most men and nearly no women smoke tobacco.”

In addition to linking indoor air pollutants to lung cancer, two studies have demonstrated a reduction in lung cancer risk associated with stove improvements. The first study, published in 2002 by Dr. Lan and colleagues at the EPA and the Chinese Academy of Preventive Medicine, showed that use of vented stoves lowered lung cancer risk by 41 percent in men and 46 percent in women and that installing a vented stove could cut indoor levels of air pollution by more than 65 percent. The second study, published in 2008, found that replacing

IARC PRODUCES ITS 100TH MONOGRAPH

The International Agency for Research on Cancer (IARC) monographs—a series of scientific reviews that evaluates chemical, physical, and micro-agents for their potential carcinogenic risks to humans—have been published annually since 1971 and have involved more than 1,000 scientists from more than 50 countries. This year, IARC takes pride in releasing its 100th volume, which reviews and updates evidence on the human carcinogens identified to date. For each agent, the volume provides a general description of exposure data; a summary of epidemiologic studies on cancer risk among humans; a summary of the experimental data, including animal bioassays; mechanistic and other relevant data; and an overall evaluation and rationale used to classify each agent for its carcinogenic potential.

To produce Volume 100, IARC convened a series of interdisciplinary working group meetings to evaluate the evidence of carcinogenicity for each agent. Several DCEG investigators participated in the reviews. **Mark Schiffman, M.D., M.P.H.**, Clinical Genetics Branch, served on the expert panel evaluating biological agents; Dr. Kenneth P. Cantor, formerly of the Occupational and Environmental Epidemiology Branch (OEEB), participated in the review of evidence for metals, arsenic, dust, and fibers; **Michael C.R. Alavanja, Dr.P.H.**, and **Qing Lan, M.D., Ph.D., M.P.H.**, both of OEEB, were members of the working group on lifestyle risk factors; and **Laura Beane Freeman, Ph.D.**, and **Nathanial Rothman, M.D., M.P.H., M.H.S.**, both of OEEB, evaluated chemical agents and related occupations.

—Alexandra Ekblom, M.P.H.

indoor stoves with portable stoves, which are filled with coal, lighted once daily outdoors, and brought indoors after visible smoke has diminished substantially, was associated with a reduction in lung cancer mortality risk of 38 percent in men and 59 percent in women. Replacing indoor stoves with

portable stoves is a cost-effective intervention that could substantially improve health in developing countries.

In studies analyzing risks according to the type of coal used, Dr. Lan and colleagues showed that coal emissions that contained the highest levels

of polycyclic aromatic hydrocarbons (PAHs) were associated with the highest lung cancer risk. In studies of gene-environment interactions, Dr. Lan reported a twofold increase in the risk of developing lung cancer among people who carried a homozygous deletion in the *GSTM1* gene, which codes for an enzyme that detoxifies PAHs. Based largely on DCEG's research on indoor air pollution, IARC classified indoor emissions from household combustion of coal as carcinogenic to humans. DCEG's findings are also being used to develop the World Health Organization Guidelines for Indoor Air Quality and to encourage improved home ventilation and replacement of coal with cleaner sources of energy for heating and cooking.

Dr. Lan discussed plans to evaluate the environmental and genetic determinants of lung cancer among women in Asia. An international consortium involving several Asian countries has been developed and will include a genome-wide association study (GWAS) of lung cancer with a special emphasis on reasons for the excess incidence of lung adenocarcinoma among females who have never smoked.

Dr. Lan concluded, "These collaborative efforts will help to better estimate dose-response relationships between lung cancer and coal-combustion products; the effects of other indoor pollutants, such as cooking oil volatiles from high-temperature wok cooking; and the interactions with inherited genetic variants." Dr. Lan hopes that these studies will lead to a more comprehensive understanding of the causal factors in lung cancer and ultimately help shape public health measures to reduce the incidence of this lethal cancer around the world. ■

—Cherie M. Vitartas, M.P.H.

DCEG FELLOWS AWARD FOR RESEARCH EXCELLENCE

The DCEG Fellows Award for Research Excellence (D-FARE) recognizes fellows who have made exceptional contributions to scientific research projects. Their contributions may include formulating the research idea, developing the study design, conducting fieldwork analysis, or interpreting the results, and the fellow must have had a major role in drafting a manuscript. Special consideration is given to projects in which fellows demonstrate growth beyond the discipline of their previous training. Awardees receive funding to present their research at a scientific meeting.



D-FARE Winners: (front) Meredith Shiels, Hannah Yang, and Huilin Li; (back) Alison Mondul, Dean Hosgood, and Stella Koutros.

The D-FARE program was established because attendance at scientific meetings is integral to the fellowship experience. The awards enable a greater number of fellows to participate in scientific meetings, where they are exposed to new scientific developments and can establish vital connections with other scientists.

Recipients were announced at the DCEG Town Meeting in October, and funds must be used by the end of the 2010 fiscal year.

The 2009 D-FARE recipients are:

H. Dean Hosgood, III, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB): *Mitochondrial DNA copy number and lung cancer risk in a prospective cohort study.*

Stella Koutros, Ph.D. (OEEB): *Pesticide exposure modifies the association between variants on chromosome 8q24 and prostate cancer.*

Huilin Li, Ph.D., Biostatistics Branch: *Using cases to strengthen inference on the association between single nucleotide polymorphisms and a secondary phenotype in genome-wide association studies.*

Alison Mondul, Ph.D., Nutritional Epidemiology Branch: *Serum retinol and risk of prostate cancer in the ATBC.*

Meredith Shiels, Ph.D., Infections and Immunoepidemiology Branch: *Age at cancer diagnosis among those with AIDS compared to the general population.*

Hannah P. Yang, Ph.D., Sc.M., Hormonal and Reproductive Epidemiology Branch: *Common genetic variation in the sex hormone metabolic pathway and endometrial cancer risk: Pathway-based evaluation of candidate genes.*

JOSEPH GASTWIRTH HONORED

Joseph L. Gastwirth, Ph.D., an adjunct investigator in the Biostatistics Branch (BB), was honored at a symposium sponsored by George Washington University in August. The symposium highlighted Dr. Gastwirth's contributions to statistical theory, statistics for economics and law, and biostatistics. Two Festschriften were published from the symposium as special issues of the journals *Statistics and Its Interface* and *Law, Probability and Risk*.

Dr. Gastwirth was a visiting scientist in BB from 1999 to 2000 and has continued to collaborate with several Branch members. In a project with **Ruth M. Pfeiffer, Ph.D.** (BB), he proposed pooling DNA samples as a means to protect confidentiality in dealing with genetic data and

to increase efficiency. Dr. Pfeiffer led the resulting work that described how to estimate joint allele frequencies at two loci, as well as a linkage disequilibrium parameter, in the presence of pooled assay misclassification.

While at BB, Dr. Gastwirth became interested in the measurement of health disparities and proposed the Peters-Belson method of regression adjustment. In this method, a large population, such as white males, is used to fit a regression model for a health-related event, such as colorectal cancer screening. This model is then used to estimate the expected values for a small subgroup, such as black males. A comparison is then made between the regression predictions and the observed health events

in the subgroup. **Barry I. Graubard, Ph.D.** (BB), and former BB fellow Dr. R. Sowmya Rao led work that showed how the Peters-Belson method could be used to interpret disparities in cancer screening rates and how the method could be adapted for data from complex surveys.

Dr. Gastwirth's other collaborative projects include power calculations for genotype- and allele-based score tests in association studies centered on families, trend tests for association with good power regardless of the mode of genetic inheritance, and modeling risk with percentiles of exposure. ■

—Mitchell H. Gail, M.D., Ph.D.

MARGARET SPITZ JOINS DCEG AS A VISITING ADVISOR

Margaret R. Spitz, M.D., M.P.H., professor and former chair of the Department of Epidemiology at The University of Texas M.D. Anderson Cancer Center, joined DCEG as a visiting advisor in September. Dr. Spitz is a luminary in molecular epidemiology and is internationally noted for her work on tobacco-related cancers. Her research focuses on interindividual variation in susceptibility to the development of lung and other tobacco-related cancers in addition to the construction of predictive risk models for determining high-risk subgroups of smokers. She co-led one of the first genome-wide association studies (GWAS) of lung cancer, identifying a region of the long arm of chromosome 15 as the "top hit." She has led and participated in Specialized Programs of Research Excellence (SPORes) for lung, prostate, and head and neck cancers as well as international consortia to advance epidemiologic research on lung cancer. Dr. Spitz has developed risk prediction models for lung cancer using epidemiologic-, clinical-,

and molecular-based biomarkers. She also published a seminal article advancing "integrative epidemiology," a concept that links genetic and other biomarkers to the study of high-risk behaviors and disease risk as well as disease progression, prognosis, and response to treatment.

Dr. Spitz, using her extensive experience and breadth of knowledge, will advise on strategies for DCEG research programs on genetic and environmental factors related to cancer etiology, including the genetics of lung cancer and nicotine dependence. She also will advise on the development and expansion of research platforms for future initiatives, including plans for an integrative epidemiology program that incorporates new initiatives in the area of pharmacogenomics. In addition, Dr. Spitz will help foster intramural and extramural collaborations, including large-scale consortial activities, and will also be available for mentoring junior investigators and providing guidance on existing fellowship programs.



Margaret Spitz addresses DCEG staff at the Division's Annual Town Meeting.

"We are honored that Dr. Spitz has agreed to work part-time in DCEG, where her wisdom and strategic advice will be invaluable in helping us to develop research directions for the future," stated **Joseph F. Fraumeni, Jr., M.D.**, Division Director.

DCEG WELCOMES VISITING SCHOLARS DRs. KOLONEL AND FONTHAM

DCEG welcomed two leading epidemiologists in the fall of 2009 as part of its Visiting Scholars Program. In September, Dr. Laurence N. Kolonel, Deputy Director of the Cancer Research Center of Hawaii, was recognized for his leadership and vision in epidemiology, particularly in the areas of racial and ethnic health disparities. In December, Dr. Elizabeth Fontham, a professor of epidemiology and Dean of the Louisiana State University (LSU) School of Public Health, was honored for her contributions to cancer epidemiology and public health. Initiated in 2004, the Visiting Scholars Program promotes intramural-extramural scientific collaboration and idea-sharing through intensive two-day visits that include a keynote seminar, scientific roundtables and discussions, one-on-one meetings, and sessions with DCEG fellows and women scientists.

Dr. Kolonel received an M.D. from Harvard Medical School and, following an internship at the University of California, San Francisco Medical Center at Mt. Zion Hospital, he obtained an M.P.H. and Ph.D. in epidemiology at the University of California, Berkeley. After serving as an epidemiologist in the United States Air Force, Dr. Kolonel joined the Cancer Research Center of Hawaii in 1974 and developed a comprehensive research program on the role of diet and nutrition in cancer etiology. Many of his studies were designed to clarify reasons for the disparities in cancer incidence among the ethnic and racial groups in Hawaii as well as explain the changing patterns of cancer among migrant populations from Asia.

For the past 16 years, Dr. Kolonel has been a principal investigator of the NCI-supported Multiethnic Cohort Study.

This landmark study, established in Hawaii and Los Angeles, California during 1993 to 1996, is composed of more than 215,000 men and women, including those of African, Asian, Latino, Native Hawaiian, and Caucasian ancestry. It is unique among existing population cohort studies in its ethnic diversity and representation of minorities.

In his Visiting Scholar seminar titled “Prostate cancer etiology: What do we really know?” Dr. Kolonel outlined the epidemiologic characteristics of prostate cancer, including the rising incidence with advancing age; the tendency to familial occurrence; the extraordinarily high incidence of latent tumors; and the striking racial variation, with relatively high rates in African Americans and low rates in Asian Americans. The available evidence for dietary risk factors was a particular focus of his lecture, but attention was also given to recent results from genome-wide association studies (GWAS) and the role of inflammation and metabolic changes as etiologic mechanisms. He concluded his talk by stressing the importance of looking at gene-environment interactions through molecular epidemiology.

During the remainder of his visit, which was hosted by **Rashmi Sinha, Ph.D.**, Nutritional Epidemiology Branch (NEB), Dr. Kolonel attended a series of discussions focusing on the nutritional epidemiology of cancer, epigenetic variation in mediating cancer risk, risk factors for prostate cancer, the association between meat consumption and the risks for certain cancers, and the future of multiethnic and minority-based cohort studies. These sessions were moderated, respectively, by DCEG scientists **Arthur Schatzkin, M.D., Dr.P.H.** (NEB), **Mitchell H. Gail, M.D.,**



Laurence Kolonel discusses the epidemiology of prostate cancer.

Ph.D., Biostatistics Branch (BB), **Christian C. Abnet, Ph.D., M.P.H.** (NEB), **Lee E. Moore, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB), **Demetrius Albanes, M.D.** (NEB), **Ann W. Hsing, Ph.D.**, Hormonal and Reproductive Epidemiology Branch, **Amanda J. Cross, Ph.D.** (NEB), **Rachael Stolzenberg-Solomon, Ph.D., M.P.H., R.D.** (NEB), and **Robert N. Hoover, M.D., Sc.D.**, Director of the Epidemiology and Biostatistics Program. Dr. Kolonel also participated in a meeting of DCEG Women Scientists, where principal investigators, staff scientists/clinicians, and fellows discussed topics related to mentoring and career advancement.

Joseph F. Fraumeni, Jr., M.D., DCEG Director, applauded Dr. Kolonel’s contributions to cancer research and for his service on important national and international committees, including the NCI Board of Scientific Counselors. About his visit, Dr. Kolonel commented, “It was a great pleasure to meet with NCI colleagues to discuss the common issues we face and the priorities for future research in cancer epidemiology and prevention.”



Elizabeth Fontham with Michael Alavanja and Joseph Fraumeni.

DCEG Visiting Scholar Dr. Fontham received a doctorate in epidemiology at Tulane University's School of Public Health and later joined the Department of Pathology at the LSU School of Medicine, where she rose to the rank of professor. Since 2004, she has been dean of the LSU School of Public Health. She has led research on a broad range of cancer risk factors, making major contributions to genetic and environmental epidemiology. Her current work focuses on etiologic studies of gastric cancer, a multicenter study of prognostic indicators of prostate cancer in African American and Caucasian men, and genetic and environment interactions influencing pancreatic cancer. She serves as the Immediate Past President of the American Cancer Society, is on the board of the Louisiana Cancer and Health Foundation, and has had many leadership positions in professional organizations. "The combination of research, education, and service that Dr. Fontham has provided has been extremely important to this country and the world," Dr. Fraumeni stated. The topic of her Visiting Scholar Seminar was "Association of *Helicobacter pylori* infection and the cancers of specific organs."

Dr. Fontham began the lecture with a history of *H. pylori* research and its relationship to gastric cancer as a "co-carcinogenic" factor. *H. pylori* infection is prevalent among 50 percent of the world's population and is linked to socioeconomic status. It is characterized by person-to-person transmission, especially among young children in crowded living situations. She pointed out the many questions about the risks associated with non-cardia gastric cancers and MALT lymphoma as well as possible relationships to esophageal, hepatocellular, pancreatic, and colorectal cancers. She stressed that bacterial virulence, genetic susceptibility, and inflammatory responses play major roles in cancer risk. Dr. Fontham indicated areas for further research, including epidemiologic and mechanistic questions about the potential association with non-gastric cancers.

During the remainder of her visit, which was hosted by **Michael C.R. Alavanja, Dr.P.H.** (OEEB), and **Debra T. Silverman, Sc.D.**, Chief of OEEB, Dr. Fontham met with investigators from DCEG and participated in a series of roundtable discussions. **H. Dean**

Hosgood, III, Ph.D. (OEEB), and Dr. Alavanja moderated a session on recent developments in lung cancer epidemiology. **Catherine Schairer, Ph.D.** (BB), led a roundtable discussion of data related to recommendations for breast mammography screening for women ages 40–49. This was followed by a discussion led by **William F. Anderson, M.D., M.P.H.** (BB), on cancer surveillance and Surveillance, Epidemiology, and End Results (SEER) registries. Dr. Fontham also met with the Upper G.I. Working Group in a discussion led by **Neal D. Freedman, Ph.D., M.P.H.** (NEB). Dr. Fontham spoke about the carcinogenicity of nitrates and other environmental pollutants in a meeting hosted by **Mary H. Ward, Ph.D.** (OEEB). Dr. Stolzenberg-Solomon hosted a discussion on pancreatic cancer, including its relation to ABO blood type, *H. pylori*, and environmental and nutritional risk factors. Dr. Fontham also met with DCEG fellows during a brown-bag lunch hosted by **Jackie Lavigne, Ph.D., M.P.H.**, Chief of DCEG's Office of Education, and participated in an OEEB fellows' roundtable hosted by **Gabriella Andreotti, Ph.D.** (OEEB). In addition, the DCEG Women Scientists Advisors hosted a lunch with Dr. Fontham, where the discussion centered on the topic of leadership development of mid- and senior-level women scientists.

Dr. Fontham concluded her visit by thanking DCEG staff and scientists. "It's been a pleasure to meet with the special mix of scientists gathered in DCEG. It has been nice to see old friends and familiar faces."

Following each Visiting Scholar Seminar, Dr. Fraumeni presented Dr. Kolonel and Dr. Fontham with DCEG Visiting Scholar Awards in recognition of their major scientific accomplishments. ■

—Alexandra Ekblom, M.P.H.

DCEG ANNUAL TOWN MEETING

Last October, DCEG held its Annual Town Meeting to celebrate the accomplishments of Division members during the past year. **Joseph F. Fraumeni, Jr., M.D.**, Division Director, welcomed the staff and featured speaker **Margaret R. Spitz, M.D., M.P.H.**, a special advisor to DCEG and professor of epidemiology at The University of Texas M.D. Anderson Cancer Center. **Shelia Hoar Zahm, Sc.D.**, DCEG Deputy Director, opened the meeting with an overview of the Division's breadth of research and a summary of significant DCEG scientific publications, including new findings generated from genome-wide association studies (GWAS). She also summarized increased activity at the Core Genotyping Facility, the DNA Extraction and Staging Laboratory, the biorepositories, and other infrastructure operations. Dr. Zahm concluded with a review of the honors and awards received by DCEG investigators, staff additions and departures, training activities, and other special events of 2009.

Dr. Fraumeni introduced Dr. Spitz to the Division, remarking, "Her exceptional scientific career and leadership in epidemiologic research place Dr. Spitz in a class by herself. She will be an asset to the Division and NCI as an advisor and mentor to junior and senior investigators and through her ability to promote intramural and extramural collaborations."

In her presentation "Evolution of molecular epidemiologic research: Where will epidemiology go in the 21st century?" Dr. Spitz outlined the progression of the field of epidemiology from classical approaches to integrative molecular epidemiology and hypothesized about the promise that GWAS may hold for

epidemiologic research. Using lung cancer as an example, Dr. Spitz illustrated how integrating molecular and genetic information with environmental exposures and lifestyle risk factors has not only led to a more comprehensive understanding of disease causation and progression but has also provided a means for improved prevention and treatment. She also described the added value genetic analysis may have for improving predictors of outcome. Dr. Spitz concluded her talk by outlining future directions that could incorporate genomic and molecular technologies into epidemiologic study designs, stating, "This is an exciting time to be a molecular epidemiologist." Following her presentation, Dr. Spitz answered questions from the audience.

Dr. Zahm then led the annual awards ceremony recognizing scientific contributions and outstanding service during the past year. The ceremony began with the Fellowship Achievement Awards, which honor fellows who have excelled during their time at DCEG and provide stipend increases at the next appointment renewal. Awards were given to **Porcia Bradford, M.D.**, Genetic Epidemiology Branch; **H. Dean Hosgood, III, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB); **Stella Koutros, Ph.D.** (OEEB); **Idan Menashe, Ph.D.**, Biostatistics Branch (BB); and **Lisa Mirabello, Ph.D.**, Clinical Genetics Branch.

DCEG Special Appreciation and Recognition Awards were given to Dr. Christine Berg, Division of Cancer Prevention, for her dedicated efforts on behalf of the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial; Dr. Kenneth P. Cantor, formerly of



Award Recipients with Joseph Fraumeni (top to bottom): Outstanding Research Paper by a Staff Scientist/Clinician Award recipients Joanne Colt and Alice Sigurdson; Outstanding Mentor Award recipients Christian Abnet and Ruth Pfeiffer; and Exemplary Service Award recipient Mark Sherman. (Photograph credit: Bill Branson)



Recipients of the Outstanding Research Paper by a Fellow Award with Joseph Fraumeni: Neal Freedman, Anil Chaturvedi, Joseph Fraumeni, Sonja Berndt, and Dean Hosgood. (Not Shown: Jiyoung Ahn and James Li.) (Photograph credit: Bill Branson)

OEEB, for his career-long contributions to the research and training programs in environmental epidemiology; **Amy Hutchinson, M.S.**, Director of Operations of the Core Genotyping Facility, for her outstanding contributions; Dr. Timothy Sheehy, SAIC-Frederick, Inc., for his work to add sample handling and Identifiler assays to the services available through the DNA Extraction and Staging Laboratory; and Monique St. Louis, NIH Office of Human Resources, for her superb and speedy work on the Division's personnel actions.

Christian C. Abnet, Ph.D., M.P.H., Nutritional Epidemiology Branch, and **Ruth M. Pfeiffer, Ph.D.** (BB), received DCEG Outstanding Mentor Awards in recognition of their exceptional commitment to the growth and productivity of junior scientists. Dr. Abnet was described as "an exceptional scientist with wide-ranging expertise, strong quantitative skills, and an infectious excitement for science." Dr. Pfeiffer was commended for her mentorship, which "extends far beyond the invaluable statistical expertise for which she is known."

The DCEG Exemplary Service Award was given to **Mark E. Sherman, M.D.**, Hormonal and Reproductive Epidemiology Branch, for his sustained research accomplishments and integration of

cutting-edge pathology components into epidemiologic studies. His work has included determining whether unique methods exist to subdivide tumors into etiologically distinct subgroups and finding ways to measure novel tissue markers. Recognizing that DCEG's archive of fixed and frozen pathology specimens was growing and that appropriate support was needed to examine tumors by molecular subtype and build tissue microarrays, Dr. Sherman developed a proposal for a specialized laboratory to provide oversight and improve quality control. He then worked to make the NCI Applied Molecular Pathology Laboratory a reality. Tissue samples from the Polish breast, endometrial, and ovarian cancer study, on which he has served as a co-investigator, are being used as the initial test specimens for this laboratory. This new resource combines the expertise of scientists from DCEG and the Center for Cancer Research and will be a critical component of future research in molecular epidemiology.

The spring 2009 winners of DCEG Intramural Research Awards, which were announced earlier in the year, also received plaques at the Annual Town Meeting. The entire event was coordinated by **Samantha Nhan**, Office of Communications and Special Initiatives. ■

Awards for Outstanding Research Paper by a Fellow or a Staff Scientist/Clinician

Six papers published in 2008 were selected for the Outstanding Research Paper by a Fellow Award, and two papers were selected for the Outstanding Research Paper by a Staff Scientist/Clinician Award. The Division's Senior Advisory Group judged the competition based on the papers' impact, innovation, and clarity of thought and language.

The 2008 winning papers by fellows are:

Jiyoung Ahn, Ph.D., Nutritional Epidemiology Branch (NEB): "Variation in *KLK* genes, prostate-specific antigen and risk of prostate cancer," *Nature Genetics*

Sonja I. Berndt, Pharm.D., Ph.D., Occupational and Environmental Epidemiology Branch (OEEB): "Pooled analysis of genetic variation at chromosome 8q24 and colorectal neoplasia risk," *Human Molecular Genetics*

Anil K. Chaturvedi, Ph.D., Infections and Immunoepidemiology Branch: "Incidence trends for HPV-related and HPV-unrelated oral squamous cell carcinomas in the U.S.," *Journal of Clinical Oncology*

Neal D. Freedman, Ph.D., M.P.H. (NEB): "Cigarette smoking and subsequent risk of lung cancer in men and women: Analysis of a prospective cohort study," *Lancet Oncology*

H. Dean Hosgood, III, Ph.D. (OEEB): "Portable stove use is associated with lower lung cancer mortality risk in lifetime smoky coal users," *British Journal of Cancer*

James Li, Ph.D., Biostatistics Branch: "Improved correction for population stratification in GWAS by identifying hidden population structures," *Genetic Epidemiology*

Winning papers by staff scientists are:

Joanne S. Colt, M.P.H., M.S. (OEEB): "Organochlorine exposure, immune gene variation, and risk of NHL," *Blood*

Alice J. Sigurdson, Ph.D., Radiation Epidemiology Branch: "Routine diagnostic X-ray examinations and increased frequency of chromosome translocation among U.S. radiologic technologists," *Cancer Research*

RACHAEL STOLZENBERG-SOLOMON SEEKS ANSWERS TO PANCREATIC CANCER

Rachael Stolzenberg-Solomon, Ph.D., M.P.H., R.D., of the Nutritional Epidemiology Branch (NEB), attributes her long-standing research interest in pancreatic cancer to both inspiration and serendipity. The inspiration to study nutrition and cancer came from her father, a reproductive physiologist who conducted toxicology research. “Through discussions with my father, I grew up aware of the concept that mutagens and other exposures in food could contribute to cancer,” Dr. Stolzenberg-Solomon recalled. The serendipity came in the 1990s, when she was working as a registered dietitian at Johns Hopkins Hospital. Dr. Stolzenberg-Solomon provided nutritional counseling and support to pancreatic cancer patients undergoing surgical resection of their tumors. “Patients with pancreatic cancer came from all over the country to be treated at Hopkins, so we saw many patients with this type of cancer,” Dr. Stolzenberg-Solomon said. “I was intrigued, because pancreatic cancer is so devastating and, yet, we had little understanding about its causes, other than a link to smoking.” She began noticing that many of the newly diagnosed patients suffered from macrocytic anemia, which may be caused by folate deficiency—an observation she went on to study as part of her doctoral dissertation work at the Johns Hopkins Bloomberg School of Public Health.

Ultimately, Dr. Stolzenberg-Solomon’s research interests led her to NCI—first as a predoctoral fellow in the Cancer Prevention Studies Branch of the former Division of Cancer Prevention and Control, later the Center for Cancer Research, and then as a postdoctoral fellow in the Division

of Cancer Prevention and DCEG. She became a tenure-track investigator in NEB in 2002.

Dr. Stolzenberg-Solomon’s epidemiologic work has focused on examining genetic, infectious, dietary, lifestyle, and other risk factors, including the presence of biomarkers, that may help reveal underlying mechanisms of carcinogenesis, particularly as they relate to pancreatic cancer. A primary approach of her research is using prospective data from cohort studies. Since 2006, Dr. Stolzenberg-Solomon’s efforts, in collaboration with other investigators at DCEG and extramurally, have focused on conducting and completing the first genome-wide association study (GWAS) for pancreatic cancer in a large-scale consortial effort (known as PanScan).

The results of this GWAS, published in the September 2009 issue of *Nature Genetics*, showed a link between the gene for ABO blood type and pancreatic cancer. “We don’t understand the mechanism by which the ABO blood type influences pancreatic cancer risk, but the association is robust,” Dr. Stolzenberg-Solomon observed. The data are consistent with findings from small studies in the 1950s and 1960s and with recent data from the Nurses’ Health Study and Health Professionals’ Follow-Up Study indicating that subjects with type O blood have a lower risk of pancreatic cancer than subjects with other blood types. “The differing ABO blood group frequencies across populations may exist because of evolutionary processes,” Dr. Stolzenberg-Solomon noted. “In that regard, a specific blood type would suggest a selective advantage, such as resistance against infection.” The GWAS and its rapid replication included



Rachael Stolzenberg-Solomon

more than 4,000 cases and 4,000 controls from 12 cohort studies and 8 case-control studies. “No cohort or case-control study could accomplish this alone,” Dr. Stolzenberg-Solomon stated. “PanScan is a multidisciplinary team effort that involves many investigators working together. Most epidemiologists interested in studying pancreatic cancer in the United States and Europe have contributed to this work.”

Dr. Stolzenberg-Solomon has authored or co-authored 70 peer-reviewed manuscripts and mentors graduate students and postdoctoral fellows. Additionally, she serves on the editorial boards of the *American Journal of Epidemiology* and *Cancer Epidemiology, Biomarkers & Prevention*. Dr. Stolzenberg-Solomon also holds a position as an adjunct associate professor at the Yale School of Public Health and is a fellow of the American College of Epidemiology.

Within the Pancreatic Cancer Cohort Consortium, Dr. Stolzenberg-Solomon and her colleagues have conducted several studies and are planning several

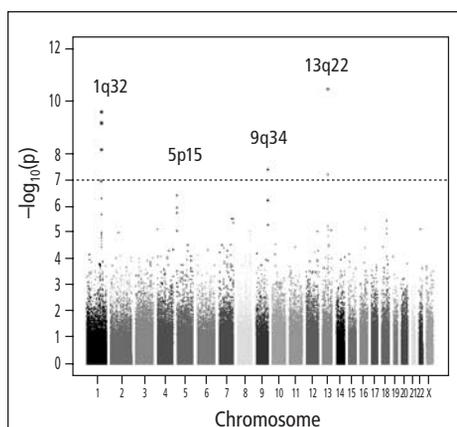


Figure 1. Manhattan plot of the p value results from the second pancreatic cancer GWAS (PanScan2) adjusted for sex, age, and population stratification.

more. The group's second GWAS on all of the participants recently identified susceptibility loci on chromosomes 1q32.1, 13q22.1, and 5p15.33. The latter maps to a region that includes the *TERT* gene that has also been linked to other cancers, including brain, lung, and bladder cancers; melanoma; and leukemia.

The scientists are conducting candidate gene pathway analyses using data from the two scans and are planning another GWAS that Dr. Stolzenberg-Solomon hopes will include an additional 1,500 new cases from the NCI Cohort Consortium. Dr. Stolzenberg-Solomon also would like to further investigate the association of pancreatic cancer with folate deficiency, a topic of her dissertation work, in collaboration with the European Prospective Investigation into Cancer and Nutrition (EPIC) team.

Dr. Stolzenberg-Solomon has won several awards in recognition of her contributions to cancer research, including a 2008 NIH Merit Award for sustained and innovative work in elucidating nutritional, genetic, infectious, and other determinants of pancreatic cancer.

Before obtaining her M.P.H. and Ph.D. degrees, she received a B.S. in dietetics

from the University of California, Davis and an M.Ed. in nutrition from Vanderbilt University. She currently represents the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Cohort Study for pancreatic cancer-related analyses in the Harvard Pooling Project on Prospective Studies of Diet and Cancer, and she serves on the steering committee for the cohort and case-control consortia on studies of pancreatic cancer.

Throughout her career at NCI—from predoctoral fellow to her current position as a tenure-track investigator—Dr. Stolzenberg-Solomon has contributed enormously to pancreatic cancer research. She remains committed to finding answers to the many questions surrounding pancreatic cancer, while simultaneously maintaining a happy and fulfilling family life with her husband and two young children. ■

—Maria Sgambati, M.D.

DCEG INVESTIGATORS PARTICIPATE IN THE NIH RESEARCH FESTIVAL

In October, DCEG members participated in the 22nd annual NIH Research Festival. This event features the achievements of intramural scientists at NIH and provides an opportunity for NIH-affiliated scientists to explore the breadth and depth of research conducted across the Intramural Research Program.

Alisa M. Goldstein, Ph.D., Genetic Epidemiology Branch (GEB), chaired a symposium titled Finding Additional High-risk Susceptibility Genes: Problems and Solutions. At the symposium, **Rose Yang, Ph.D., M.P.H.** (GEB), presented "Identification of major susceptibility genes using combined linkage and array-CGH analyses."

Poster presentations included:

William F. Anderson, M.D., M.P.H., Biostatistics Branch (BB), *Male breast cancer: A population-based comparison with female breast cancer*

Joseph Boland and Victor Lonsberry, both of the Core Genotyping Facility, *Alternate multiplex process increases flexibility of the Fluidigm integrated fluidic circuits single nucleotide polymorphism genotyping platform*

Porcia T. Bradford, M.D. (GEB), *Increased risk of secondary primary cancers after diagnosis of melanoma*

Charles Chung, Ph.D., Laboratory of Translational Genomics (LTG), *Fine-mapping of the prostate cancer locus on chromosome 11q13 reveals three independent common variants in CGEMS (Cancer Genetic Markers of Susceptibility)*

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

Sara Karami, Ph.D. (OEEB), *Family history of cancer and renal cell cancer risk in Caucasians and African Americans*

Idan Menashe, Ph.D. (BB), *Pathway analysis of breast cancer genome-wide association study (GWAS) highlights three pathways and two canonical signaling cascades*

Hemang Parikh, Ph.D. (LTG), *A comprehensive resequence analysis of the *KLK15-KLK3-KLK2* locus on chromosome 19q13.33*

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

ROSE YANG SEEKS AND FINDS CANCER SUSCEPTIBILITY GENES

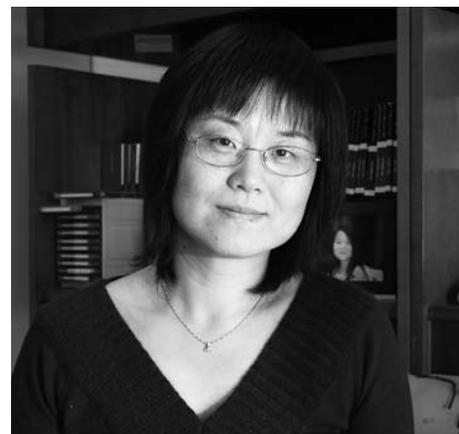
“We have spent more than 10 years searching for the genes implicated in familial chordoma,” stated **Xiaohong Rose Yang, Ph.D., M.P.H.**, an investigator in DCEG’s Genetic Epidemiology Branch (GEB). Dr. Yang is the first author of an article published in the November 2009 issue of *Nature Genetics* that identifies the duplication of a specific gene as a major susceptibility factor for familial chordoma, a rare form of bone tumor. “New technology that complemented our traditional gene-mapping strategy enabled us to make this critical discovery.”

Using this new technology—high-resolution array-based comparative genomic hybridization (array-CGH)—Dr. Yang and her colleagues analyzed the entire human genome of members of chordoma-affected families to identify unique variations in the number of gene copies present. The researchers found duplicated DNA in chromosome region 6q27 in all chordoma-affected subjects among four chordoma families. The duplicated region contained only one known gene, *T* (brachyury), which is expressed

specifically in cells from which chordoma is believed to originate. “We feel great satisfaction in having finally identified the gene after years of research,” Dr. Yang said. “Importantly, our study demonstrates that rare copy number variations (CNVs), in addition to small sequence changes, can play an important role in the development of cancer.”

Dr. Yang came to the United States to receive a Ph.D. in physiology from Georgetown University Medical Center after receiving an M.S. in cell biology at Beijing Normal University in China. Her interest in epidemiology led her to GEB as a postdoctoral fellow in 2000, during which time she received an M.P.H. from the Johns Hopkins Bloomberg School of Public Health. Since 2006, Dr. Yang has been a tenure-track investigator and has continued working on projects that expand on her postdoctoral research.

Dr. Yang believes that the identification of susceptibility genes for rare familial cancers, such as chordoma, might lead to the identification of



Rose Yang

new genes or pathways that play a role in more common cancers. Studying cancers with known hereditary links also helps researchers discern the differences between the contributions of genes and environment.

The genetic alteration that Dr. Yang found in chordoma has proven to be an interesting twist in cancer susceptibility. The discovery that an inherited duplication of a gene, rather than small sequence changes, is responsible for the development of a familial form of cancer is an important finding in the field. Dr. Yang said, “Although it is not clear how frequent and through what mechanism CNVs could influence cancer, it is possible that this type of variant is much more common in cancer than originally thought.”

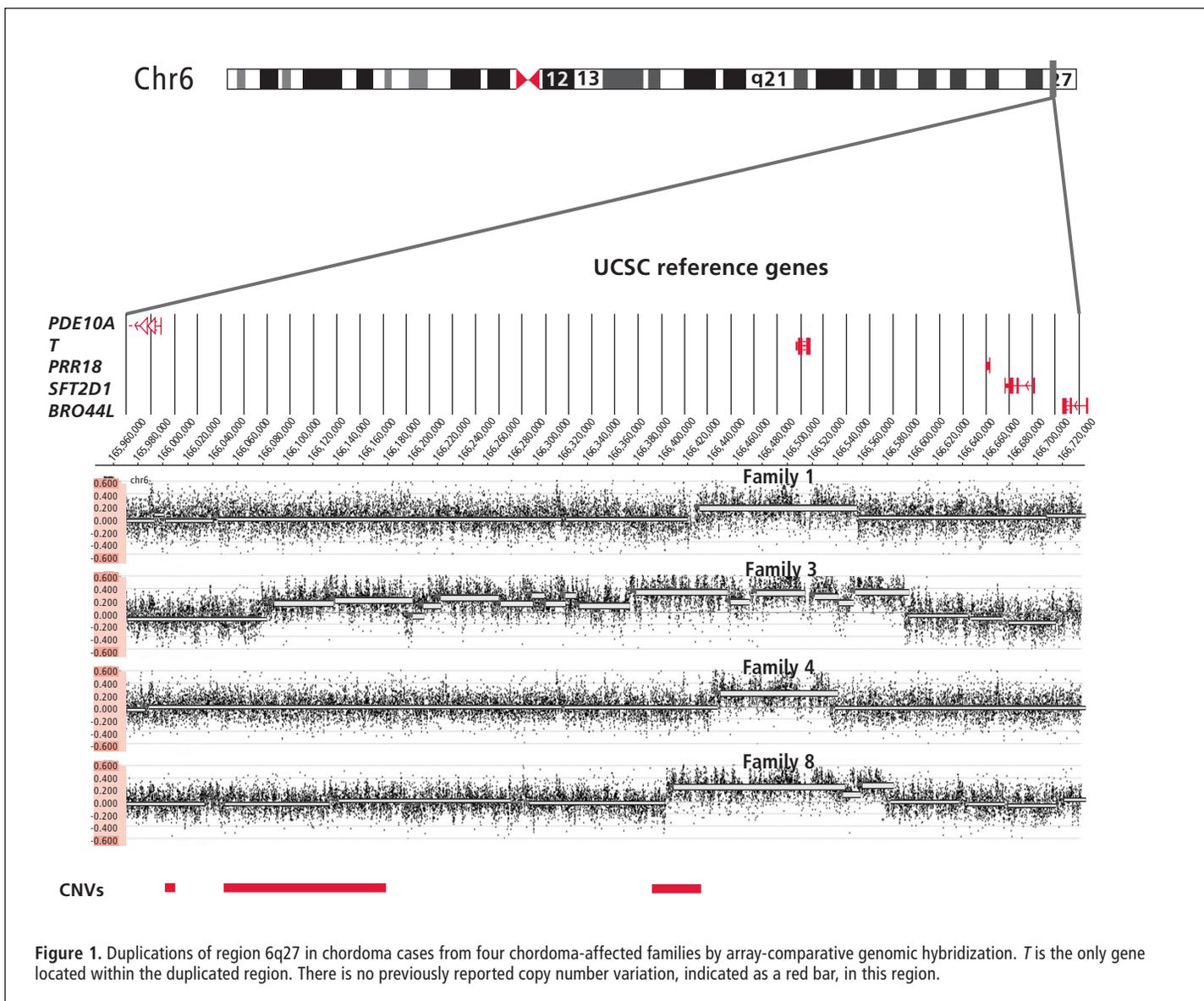
Dr. Yang is applying the techniques successfully used in the study of chordoma to determine whether CNVs may contribute to susceptibility to other inherited cancers, such as cutaneous malignant melanoma. She is employing new technologies in addition to array-CGH, such as exome sequencing, to enhance her search for genes linked to cancer susceptibility.

NEW WSA REPRESENTATIVES

Patricia Hartge, Sc.D., Epidemiology and Biostatistics Program, and **Mary H. Ward, Ph.D.**, Occupational and Environmental Epidemiology Branch, have been elected as DCEG’s new Women Scientists Advisor (WSA) and WSA-Alternate, respectively. They are replacing outgoing WSA **Ann W. Hsing, Ph.D.**, Hormonal and Reproductive Epidemiology Branch. During her three-year term as WSA, Dr. Hsing led many special initiatives, including a time management course and brown bag meetings with visiting scientists. She served on DCEG’s Senior Advisory Group and on numerous search committees as well as worked with the Center for Cancer Research representatives to develop new WSA mentoring and leadership awards. DCEG Director **Joseph F. Fraumeni, Jr., M.D.**, thanks Dr. Hsing for her dedicated service and welcomes Drs. Hartge and Ward in their new roles.



New WSA Representatives: Patricia Hartge and Mary Ward.



As part of her research portfolio, Dr. Yang works with scientists in other branches of the Division. For example, Dr. Yang and researchers in the Hormonal and Reproductive Epidemiology Branch are using tissue microarray analysis to study the etiologic heterogeneity of breast cancer. By analyzing data from a large, population-based case-control study of breast cancer, the team found that some risk factors for breast cancer differ by tumor subtypes. Dr. Yang is currently expanding this work by analyzing data pooled by the Breast Cancer Association Consortium from 34 studies of breast cancer.

Dr. Yang also leads a study—in collaboration with scientists in the Radiation Epidemiology Branch and the NCI Center for Cancer Research—on the characterization of genomic alterations in radiation-related breast cancer. Using samples collected from the Childhood Cancer Survivor Study, Dr. Yang seeks to better understand breast cancer among patients who received high-dose radiation as a treatment for childhood cancers.

Dr. Yang has received numerous awards, including the NCI Director’s Intramural Innovation Award in 2007 and 2009

for supplemental funds to support highly creative research. She credits the work environment at DCEG as part of her success. “I feel fortunate to have outstanding colleagues here at DCEG,” Dr. Yang noted. “Many of them have served as mentors. They have assisted me in making connections for research collaborations and finding appropriate resources to carry out my research.” ■

—Amber K. Boehm, Ph.D.

JACK CUZICK VISITS AS AN HREB DISTINGUISHED LECTURER

The Hormonal and Reproductive Epidemiology Branch (HREB) hosted Dr. Jack Cuzick in December as an HREB Distinguished Lecturer. Dr. Cuzick is the John Snow Professor of Epidemiology at Wolfson Institute of Preventive Medicine at Queen Mary, University of London and head of the Centre for Epidemiology, Mathematics, and Statistics at Cancer Research UK in London. He is internationally recognized for his contributions to cervical cancer screening and breast cancer chemoprevention.

During his visit, Dr. Cuzick presented a seminar titled “Chemoprevention of breast cancer: Risk factors and potential agents.” He argued that mammographic density may be the most important target for breast cancer prevention and that the key to prevention is identifying both high-risk women and non-toxic, effective preventive agents. Dr. Cuzick summarized the chemopreventive effects of

aromatase inhibitors, tamoxifen, and raloxifene in randomized trials. In addition, he described his recent findings from the International Breast Cancer Intervention Study (IBIS-I), a trial of tamoxifen for breast cancer prevention, which showed a change in mammographic density as a biomarker of risk reduction. Dr. Cuzick is currently leading IBIS-II, a large international breast cancer prevention trial that continues the work of IBIS-I. The trial, which is recruiting participants through 2011, will compare the aromatase inhibitor anastrozole with tamoxifen. Dr. Cuzick concluded his presentation by emphasizing that in addition to developing early detection technologies, future research should focus on prevention strategies that alter the natural history of breast cancer.

Following the seminar, Dr. Cuzick held a lunch discussion with DCEG



Jack Cuzick receives HREB Distinguished Lecture poster from Branch Chief Louise Brinton.

fellows that focused on early career development. His advice for fellows was to: (1) become an expert in a single cancer, (2) try to answer the major health problems, even if it takes a long time, (3) identify and work in areas that are understudied, (4) acquire a specialist skill that is in short supply, and (5) strive to be the best.

Dr. Cuzick also participated in a series of roundtable discussions moderated by HREB investigators. **Mark E. Sherman, M.D.**, led a session on breast cancer precursors and pathology; **Philip E. Castle, Ph.D., M.P.H.**, and **Nicolas Wentzensen, M.D., Ph.D.**, facilitated a discussion related to cervical cancer screening for low- and high-resource settings; **Ann W. Hsing, Ph.D.**, moderated a session on prostate cancer screening and etiologic research; and **Gretchen L. Gierach, Ph.D.**, facilitated a session on mammographic density as a “breast biosensor.” ■

—Gretchen L. Gierach, Ph.D.

INVESTIGATORS MEET TO DISCUSS CANCER IN AFRICA

DCEG researchers participated in the seventh international conference of the African Organisation for Research and Training in Cancer (AORTIC) held in Dar Es Salaam, Tanzania in November. The theme of the conference, Cancer in Africa – the New Reality, focused on all aspects of cancer care and management, from prevention and diagnosis to treatment and palliation. Special emphasis was given to cancers with unique incidence patterns, including HIV-associated cancers, cervical cancer, Kaposi sarcoma, and Burkitt’s lymphoma, as well as cancers that often are detected at unusually late stages in Africa, such as breast and prostate cancers.

Approximately 700 people attended the conference, including representatives from 36 African and 16 non-African countries. **Louise A. Brinton, Ph.D.**, Chief of the Hormonal and Reproductive Epidemiology Branch, participated in the Methods in Clinical Cancer Research Workshop, sponsored by the American Society of Clinical Oncology (ASCO), and gave a presentation entitled “Good ideas, poor outcomes: Avoiding the pitfalls of epidemiologic research.” **Sam M. Mbulaiteye, M.D.**, Infections and Immunoepidemiology Branch, held a stakeholders’ meeting for NCI’s Epidemiology of Burkitt’s Lymphoma in East African Children or Minors (EMBLEM) study with collaborators from Tanzania and Kenya.

—Louise A. Brinton, Ph.D., and Sam M. Mbulaiteye, M.D.

CONSORTIUM FORMS TO STUDY LUNG CANCER IN ASIA

Most cases of lung cancer among East Asian women occur among never smokers; this high cancer rate suggests that genetic/environmental risk factors are involved. **Qing Lan, M.D., Ph.D., M.P.H.**, and **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, both of the Occupational and Environmental Epidemiology Branch (OEEB), hosted investigators from mainland China, Taiwan, Singapore, Japan, and the Republic of Korea at a meeting at NCI in December to develop research plans to study the etiology of lung cancer among never-smoking women in Asia. **Joseph F. Fraumeni, Jr., M.D.**, Division Director, provided introductory comments at the meeting and described this multinational effort as “a study that will be viewed as a landmark event in lung cancer research.”

The meeting opened with a discussion of the first planned consortia project, a genome-wide association study (GWAS) of lung cancer among never-smoking Asian women. This work follows genome-wide scans that were recently completed in Caucasian populations, primarily among smokers, and will provide an opportunity to determine whether variants previously identified in Western populations are also present in this population. Additionally, a GWAS among never-smoking women in Asia has the potential to identify unique genetic variants in this population, where risk is driven partially by environmental factors other than tobacco, such as in-home solid fuel use and oil fumes from cooking. Following this discussion, Dr. Lan summarized an initial GWAS replication effort that found a region in the *TERT-CLPTMIL* locus on chromosome 5p15 to be associated with risk of lung adenocarcinoma among never-smoking women in Asia. This result

parallels findings from a recent GWAS in Caucasians reported by **Maria Teresa Landi, M.D., Ph.D.**, and **Neil E. Caporaso, M.D.**, of the Genetic Epidemiology Branch. **H. Dean Hosgood, III, Ph.D.** (OEEB), presented a meta-analysis suggesting that the *GSTM1* null genotype plays a role in lung cancer etiology in Asian populations exposed to indoor combustion products of coal used for cooking and heating; this contrasts with the inconsistent findings for this genotype reported in studies among Caucasians. **Stephen J. Chanock, M.D.**, Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, reported on the current and future outlook of GWAS

research studies. The meeting then focused on finalization of the protocol for the GWAS effort. Agreement was reached to include smoking women in the GWAS as well as data on epidermal growth factor receptor (EGFR) mutation status of tumors and survival. Study investigators agreed to incorporate a core environmental exposure questionnaire into the many studies that are still enrolling subjects for use in future analyses of gene-environment interactions. A coordinating committee with representatives from each participating study was established to further the goals of the consortium. ■

—Qing Lan, M.D., Ph.D., M.P.H.

NEW SALLIE ROSEN KAPLAN FELLOW

Britton Trabert, Ph.D., recently joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a Sallie Rosen Kaplan Postdoctoral Fellow. NCI awards the Sallie Rosen Kaplan Fellowship for Women Scientists in Cancer Research through an annual competition among postdoctoral fellows applying to train in the NCI Intramural Research Program. Made possible by a bequest from Ms. Kaplan to the Foundation for NIH, the women scientists receive a supplement to their first-year stipend.

Dr. Trabert comes to HREB from the University of Washington School of Public Health, where she earned a Ph.D. in epidemiology under the guidance of Dr. Victoria L. Holt. Her dissertation research sought to identify risk factors for endometriosis. Previously, Dr. Trabert completed an M.S.P.H. in epidemiology at the Emory University Rollins School of Public Health and an M.S. in biostatistics from the University of Michigan School of Public Health. Within DCEG, Dr. Trabert will continue to pursue her interests in reproductive and life-course epidemiology by focusing on hormone-related tumors in both men and women. She has begun working with **Katherine A. McGlynn, Ph.D.**, a senior investigator in HREB, to examine hormonal and genetic influences on the etiology of testicular cancer and other conditions associated with testicular dysgenesis syndrome. Toward this end, Dr. Trabert is analyzing data from the Servicemen's Testicular Tumor Environmental and Endocrine Determinants (STEED) Study and the NIH Collaborative Perinatal Project. Dr. Trabert has also begun working with **Louise A. Brinton, Ph.D.**, Chief of HREB, to examine risk factors for endometrial cancer and the cancer risks associated with infertility treatments.



Britton Trabert

AN UPDATE ON THE INTERLYMPH CONSORTIUM

The InterLymph Consortium Eighth Annual Meeting was held in July at the University of British Columbia (UBC) in Vancouver. Formed in 2001, the InterLymph Consortium is an international group of investigators who conduct case-control studies of non-Hodgkin lymphoma (NHL). Consortium members discuss research, undertake projects that pool data across studies, and participate in collaborative research. This year's meeting included sessions to develop specific collaborative projects, including new consortia for Hodgkin lymphoma (HL) and multiple myeloma (MM) research. Sixty-nine researchers from 13 countries attended meeting workshops. **Martha S. Linet, M.D., M.P.H.**, Chief of the Radiation Epidemiology Branch, and **Patricia Hartge, Sc.D.**, Epidemiology and Biostatistics Program, received awards for their outstanding service and their roles in founding the InterLymph Consortium.

Nathaniel Rothman, M.D., M.P.H., M.H.S., Occupational and Environmental Epidemiology Branch, and **Stephen J. Chanock, M.D.**, Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, organized and cochaired a two-day meeting of researchers who are collaborating on a genome-wide association study (GWAS) of NHL. Discussions included whether to scan all cases versus histological subtypes, replication strategies, IRB requirements and NIH policies, DNA specifications, statistical approaches to analyses, and opportunities to leverage data on controls from previous GWAS scans. Participants agreed to supplement the etiologic study with a survival component. The group also established a GWAS Coordination Committee to include representatives from each participating NHL study as well as a publications subcommittee and an analysis working group.



InterLymph Consortium Eighth Annual Meeting participants. (Photograph credit: Neil Edwardson, Arthur Edwardson Photography)

Working groups laid out plans for gene-environment analyses to include evaluation of autoimmune factors, tobacco use, hair dye use, body mass index, height, familial occurrence, and occupational and environmental history as well as analyses of risk factors for rare NHL subtypes and survival. Dr. Christine Skibola of the University of California, Berkeley discussed InterLymph governance, including the project proposal and membership application process. Since the last InterLymph meeting in Australia, two major efforts were launched. First, a data coordinating center, established under the leadership of Dr. Susan Slager of the Mayo Clinic, provides centralized, well-documented approaches for combining datasets, creates a comprehensive data dictionary, develops core variables, and provides assistance and guidance on the more complex statistical analyses. Second, an InterLymph survey, for which Dr. Slager provided preliminary results, was conducted to provide information on cases with specific histopathological subtypes, genotyping efforts, specific genetic pathways, and variables from individual studies.

The HL Working Group meeting—co-led by Dr. Wendy Cozen of the University of Southern California,

Dr. Sally Glaser of the Northern California Cancer Center, and Dr. Henrik Hjalgrim of the Statens Serum Institute—included presentations on a new susceptibility gene for HL, cytokine profiles in prediagnostic serum samples, and variations in methylation in twins discordant for HL. New studies are planned, and two pooling projects will soon be ending. The working group also plans to write a position paper on HL and Epstein-Barr virus.

The MM Working Group, led by Dr. Brenda Birmann of Brigham and Women's Hospital and Harvard Medical School, included presentations on the role of monoclonal gammopathy of undetermined significance and other risk factors. The working group also discussed plans for a member survey to ascertain data available for pooled collaborative studies to identify genetic susceptibility, lifestyle and environmental exposures, and gene-environment interactions.

Dr. John Spinelli, UBC, and Dr. Angela Brooks-Wilson, Simon Fraser University, organized the meeting. The next InterLymph Annual Meeting will be held in Washington, DC in April 2010. ■

—Annelie M. Landgren, M.P.H.

COHORT CONSORTIUM CONVENES ANNUAL MEETING

Investigators representing 39 cohort studies from the United States and abroad came together in Bethesda, Maryland in November for the NCI Cohort Consortium's annual meeting. **Joseph F. Fraumeni, Jr., M.D.**, DCEG Director, and Dr. Robert Croyle, Director of NCI's Division of Cancer Control and Population Sciences (DCCPS), welcomed the participants and congratulated the group on 10 years of ground-breaking research that has combined the rapid advances in genomics with the power of rigorously designed cohort studies. Co-founder **Robert N. Hoover, M.D., Sc.D.**, Director of the Epidemiology and Biostatistics Program (EBP), recognized outgoing chair **Patricia Hartge, Sc.D.** (EBP), for her years of leadership and service. He congratulated her successor, Dr. Michael Thun of the American Cancer Society, and welcomed new secretariat member Dr. Julie Buring of Brigham and Women's Hospital and Harvard Medical School. He also thanked **Geoffrey Tobias**, Human Genetics Program, for his work as communications coordinator and welcomed Scott Rogers of DCCPS to the secretariat as NCI cohort liaison.

Dr. Hartge provided an overview of the past year, citing the progress made in the consortium's many initiatives, including the activities of four major projects: the Breast and Prostate Cancer Cohort Consortium (BPC3) identified genetic variants related to each cancer, published extensively, and launched a genome-wide association study (GWAS) of estrogen receptor-negative breast cancer and advanced prostate cancer; the Pancreatic Cancer Cohort Consortium (PanScan) identified variants in the ABO blood type gene and several other loci related to cancer risk, quantified risks associated with other factors,



Secretariat Members: (front) Robert Croyle, Joseph Fraumeni, and Robert Hoover; (back) Nonye Harvey, Michael Thun, Patricia Hartge, Julie Palmer, Deborah Winn, Anne Zeleniuch-Jacquotte, Julie Buring, and James Cerhan. (Photograph credit: Keith Richardson)

and explored the joint effects of genes and environment; the serum-based Vitamin D Pooling Project (VDPP) submitted results on six cancers for publication *en bloc*; and the results from the Obesity and Mortality Pooling Project will be submitted for publication shortly.

Stephen J. Chanock, M.D., Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, chaired a scientific panel discussion devoted to future directions in genomic studies. Presentations included a talk on integrated analyses of quantitative trait loci in neurological disease; an overview of the "ClinSeq" pilot project, which correlates genetic risk variants with disease phenotypes; and an examination of the difficulties in finding a genetic basis for some highly heritable traits. Some of the participants suggested that gene-gene or gene-environment interactions might obscure associations using GWAS, even in large-scale studies that include the NCI Cohort Consortium.

The second plenary session focused on biobanking, proteomics, and biomarkers. Participants discussed several topics, including how future cohort studies could employ biospecimens to bridge the gap between population and disease cohorts and use well-characterized biomarkers to inform therapeutic interventions; the promise of proteomics for such applications as identifying early detection markers; and key features of population biobank projects that the consortium could undertake, such as studies of rare cancers, use of high-density data (e.g., genomics, proteomics, metabolomics), and areas of pressing public health concern (e.g., the role of folate in cancer development). The meeting ended with a strategic planning workshop.

To learn more about the Cohort Consortium, including its research and working groups, go to <http://epi.grants.cancer.gov/Consortia/cohort.html>. ■

—Patricia Hartge, Sc.D.,
and Alexandra Ekblom, M.P.H.

SCIENTIFIC HIGHLIGHTS

BLADDER CANCER

DNA Repair Genes and Smoking

To study the roles of smoking and DNA repair genes as risk factors for bladder cancer, meta- and pooled analyses were conducted as part of the International Consortium of Bladder Cancer. The results included data on 10 single nucleotide polymorphisms (SNPs) corresponding to 7 DNA repair genes among 5,282 cases and 5,954 controls of non-Latino, white origin. Weak but consistent associations were observed with *ERCC2 D312N* (rs1799793, per-allele odds ratio [OR] = 1.10), *NBN E185Q* (rs1805794, per-allele OR = 1.09), and *XPC A499V* (rs2228000, per-allele OR = 1.10). The association with *NBN E185Q* was limited to ever smokers and was strongest for the highest levels of smoking dose and smoking duration.

(Stern MC, Lin J, Figueroa JD, Kelsey KT, Kiltie AE, Yuan JM, Matullo G, Fletcher T, Benhamou S, Taylor JA, Placidi D, Zhang ZF, Steineck G, Rothman N, Kogevinas M, Silverman D, Malats N, Chanock S, Wu X, Karagas MR, Andrew AS, Nelson HH, Bishop DT, Sak SC, Choudhury A, Barrett JH, Elliot F, Corral R, Joshi AD, Gago-Dominguez M, Cortessis VK, Xiang YB, Gao YT, Vineis P, Sacerdote C, Guarrera S, Polidoro S, Allione A, Gurrzau E, Koppova K, Kumar R, Rudnai P, Porru S, Carta A, Campagna M, Arici C, Park SS, Garcia-Closas M, International Consortium of Bladder Cancer. Polymorphisms in DNA repair genes, smoking, and bladder cancer risk: Findings from the International Consortium of Bladder Cancer. *Cancer Res* 2009;69:6857–6864)

Rising Trend in Smoking-induced Tumors

The authors studied bladder cancer risk in relation to smoking using interview data from a population-based, case-control study conducted in Maine, New Hampshire, and Vermont from 2001 to 2004 among 1,170 urothelial carcinoma patients and 1,413 controls. The study

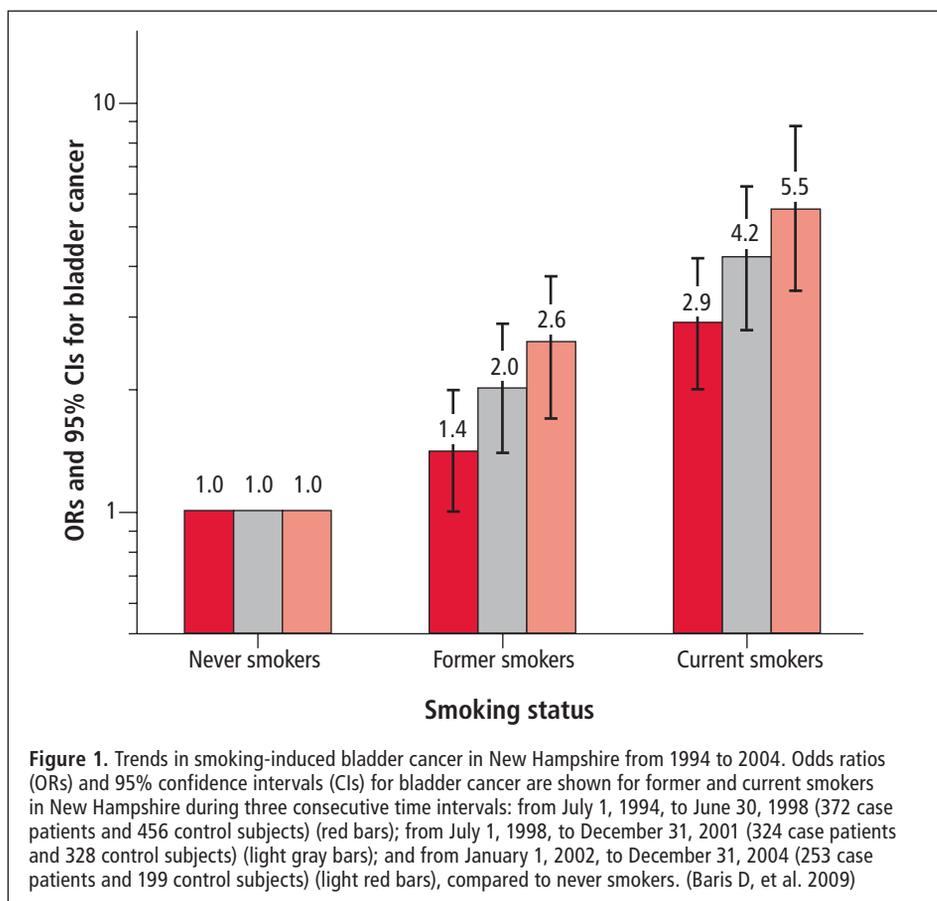


Figure 1. Trends in smoking-induced bladder cancer in New Hampshire from 1994 to 2004. Odds ratios (ORs) and 95% confidence intervals (CIs) for bladder cancer are shown for former and current smokers in New Hampshire during three consecutive time intervals: from July 1, 1994, to June 30, 1998 (372 case patients and 456 control subjects) (red bars); from July 1, 1998, to December 31, 2001 (324 case patients and 328 control subjects) (light gray bars); and from January 1, 2002, to December 31, 2004 (253 case patients and 199 control subjects) (light red bars), compared to never smokers. (Baris D, et al. 2009)

examined changes in smoking-induced bladder cancer risk over time by comparing ORs from New Hampshire residents in this study with those from two earlier case-control studies conducted there (see Figure 1). Regular and current cigarette smokers had higher risks of bladder cancer than never smokers (regular smokers, OR = 3.0; current smokers, OR = 5.2). There was an increasing trend in smoking-related risks over three consecutive periods (1994–1998, 1998–2001, and 2002–2004) among former smokers (OR = 1.4, 2.0, and 2.6, respectively) and current smokers (OR = 2.9, 4.2, and 5.5, respectively). Within categories of intensity, ORs increased approximately linearly with increasing pack-years smoked, but the slope of the increasing trend for smoking-related risks declined with increasing intensity. Based on modeling

of pack-years and intensity, with equal pack-years of cigarettes smoked, smoking fewer cigarettes over a long time appeared more harmful than smoking more cigarettes over a shorter time. (Baris D, Karagas MR, Verrill C, Johnson A, Andrew AS, Marsit CJ, Schwenn M, Colt JS, Cherala S, Samanic C, Waddell R, Cantor KP, Schned A, Rothman N, Lubin J, Fraumeni JF Jr, Hoover RN, Kelsey KT, Silverman DT. A case-control study of smoking and bladder cancer risk: Emergent patterns over time. *J Natl Cancer Inst* 2009;101:1553–1561)

BRAIN TUMORS

Height, Body Mass Index, and Physical Activity

Height, body mass index (BMI), and physical activity were studied in relation to glioma risk in the prospective NIH-AARP Diet and Health Study.

Participants completed a baseline questionnaire sent in 1995–1996 inquiring about height, weight, and potential confounders. A second questionnaire sent in 1996 inquired about physical activity at ages 15–18, 19–29, and 35–39 years, as well as during the past 10 years, and weight at ages 18, 35, and 50 years. During follow-up through 2003, 480 cases of glioma among 499,437 respondents to the baseline questionnaire and 257 cases among 305,681 respondents to the second questionnaire were documented. Glioma risk among tall persons (≥ 1.90 m) was twice that of short persons (< 1.60 m) (multivariate relative risk [RR] = 2.12). Risk among participants who were obese (BMI 30.0–34.9 kg/m²) at age 18 years was nearly four times that of persons of normal weight (BMI 18.5–24.9 kg/m²) at this age (RR = 3.74). Risk among participants who were active during ages 15–18 years was 36% lower than that of persons who were inactive. BMI and physical activity after age 18 years were unrelated to glioma risk. Results support a role for early-life energy balance in glioma carcinogenesis. (Moore SC, Rajaraman P, Dubrow R, Darefsky AS, Koebnick C, Hollenbeck A, Schatzkin A, Leitzmann MF. Height, body mass index, and physical activity in relation to glioma risk. *Cancer Res* 2009;69:8349–8355)

BREAST CANCER

Müllerian Inhibiting Substance Levels

To examine whether serum Müllerian inhibiting substance (MIS) levels are associated with breast cancer risk, the authors conducted a prospective case-control study of 309 participants registered in the Columbia, Missouri Serum Bank. Each of 105 *in situ* or invasive breast cancer cases with prediagnostic serum collected before menopause was matched to two control subjects by age, date, menstrual cycle day, and time of day of blood collection. The relative ORs of breast cancer for women in

increasing MIS quartiles were 1, 2.8, 5.9, and 9.8 ($p < 0.001$). The association was weaker in women who were not taking oral contraceptives at the time of blood collection, but adjustment for estradiol and testosterone levels did not materially alter results. The association of MIS with breast cancer did not vary by age at blood collection but was stronger among women diagnosed with breast cancer at an older age than among those diagnosed at a younger age. MIS may be a novel biomarker of increased breast cancer risk. (Dorgan JF, Stanczyk FZ, Egleston BL, Kahle LL, Shaw CM, Spittle CS, Godwin AK, Brinton LA. Prospective case-control study of serum Müllerian inhibiting substance and breast cancer risk. *J Natl Cancer Inst* 2009;101:1501–1509)

Risk Related to Childhood Cancer Treatments

Conducting a case-control study of breast cancer in a cohort of 6,647 women who were five-year survivors of childhood cancer treated during 1970–1986, the authors identified 120 patients with histologically confirmed breast cancer and matched each patient to four controls by age at and time since initial cancer. The OR for breast cancer increased linearly with radiation dose and reached 11-fold for local breast doses of about 40 Gy relative to no radiation. Risk associated with breast irradiation was sharply reduced among women who received 5 Gy or more to the ovaries. The excess OR per Gy was 0.36 for those who received ovarian doses less than 5 Gy and 0.06 for those who received higher doses. Radiation-related risk did not vary significantly by age at exposure. Use of dacarbazine, dactinomycin, doxorubicin, and carmustine showed borderline significantly elevated risks. Results confirm the radiation sensitivity of the breast in females ages 10–20 years old but do not show a strong effect of age at exposure within this range. Irradiation of the ovaries at doses of 5 Gy or greater seems

to lessen the carcinogenic effects of breast irradiation. (Inskip PD, Robison LL, Stovall M, Smith SA, Hammond S, Mertens AC, Whitton JA, Diller L, Kenney L, Donaldson SS, Meadows AT, Neglia JP. Radiation dose and breast cancer risk in the childhood cancer survivor study. *J Clin Oncol* 2009;27:3901–3907)

GENETICS

Familial Chordoma

Using high-resolution, array-comparative genomic hybridization analysis, the authors identified unique duplications of a region on chromosome 6q27 in four multiplex families with at least three cases of chordoma, a cancer of presumed notochordal origin. The duplicated region contains only the *T* (brachyury) gene, which is important in notochord development and is expressed in most sporadic chordomas. These findings highlight the value of screening for complex genomic rearrangements in searches for cancer susceptibility genes. (Yang XR, Ng D, Alcorta DA, Liebsch NJ, Sheridan E, Li S, Goldstein AM, Parry DM, Kelley MJ. *T* (brachyury) gene duplication confers major susceptibility to familial chordoma. *Nat Genet* 2009;41:1176–1178)

A New Statistic for Genome-wide Association Studies

Aggregate results from genome-wide association studies (GWAS), such as genotype frequencies for cases and controls, were often made available on public web sites until recently due to an assumption that such results disclosed negligible personal information. A recent study suggested that a method for forensic detection of an individual's contribution to an admixed DNA sample could be applied to aggregate GWAS data (Homer N, et al. Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. *PLoS Genet* 2008;4:e1000167). Using a likelihood-based statistical framework,

the authors developed an improved statistic that uses genotype frequencies and individual genotypes to infer whether a specific individual or any close relatives participated in the GWAS and, if so, the participant's phenotype status. This statistic compares the logarithm of genotype frequencies, in contrast to that of Homer et al., which is based on differences in either SNP probe intensity or allele frequencies. The authors also derived the theoretical power of their test statistics and explored empirical performance in scenarios with varying numbers of randomly chosen or top-associated SNPs. (Jacobs KB, Yeager M, Wacholder S, Craig D, Kraft P, Hunter DJ, Paschal J, Manolio TA, Tucker M, Hoover RN, Thomas GD, Chanock SJ, Chatterjee N. A new statistic and its power to infer membership in a genome-wide association study using genotype frequencies. *Nat Genet* 2009;41:1253–1257)

HEAD AND NECK CANCERS

Smoking and Alcohol Consumption

The authors pooled data from 15 case-control studies and modeled the excess odds ratio (EOR) to assess the risks of laryngeal, pharyngeal, and oral cavity cancers by total cigarette smoke and alcohol exposure (pack-years and drink-years) and the modification of risks by exposure rate (cigarettes/day and

drinks/day). Above 15 cigarettes per day, the EOR per pack-year decreased with increasing cigarettes per day, suggesting that more cigarettes per day for a shorter duration was less deleterious than fewer cigarettes per day for a longer duration. Estimates of EOR per pack-year were homogeneous across sites, whereas the effects of cigarettes per day varied, indicating that the greater laryngeal cancer risk derived from differential cigarettes per day effects and not pack-years. EOR per drink-year estimates increased through 10 drinks per day, suggesting that greater drinks per day for a shorter duration was more deleterious than fewer drinks per day for a longer duration. EOR per drink-year estimates varied by site, whereas drinks per day effects were homogeneous, indicating that the greater pharyngeal and oral cavity cancer risk with alcohol consumption derived from the differential effects of drink-years and not drinks per day. (Lubin JH, Purdue M, Kelsey K, Zhang ZF, Winn D, Wei Q, Talamini R, Szeszenia-Dabrowska N, Sturgis EM, Smith E, Shangina O, Schwartz SM, Rudnai P, Neto JE, Muscat J, Morgenstern H, Menezes A, Matos E, Mates IN, Lissowska J, Levi F, Lazarus P, La Vecchia C, Koifman S, Herrero R, Franceschi S, Wünsch-Filho V, Fernandez L, Fabianova E, Daudt AW, Maso LD, Curado MP, Chen C, Castellsague X, Brennan P,

Boffetta P, Hashibe M, Hayes RB. Total exposure and exposure rate effects for alcohol and smoking and risk of head and neck cancer: A pooled analysis of case-control studies. *Am J Epidemiol* 2009;170:937–947)

KIDNEY CANCER

Apolipoprotein E/C1 Locus Variants

The investigators genotyped 635 SNPs in 38 candidate lipid peroxidation genes in 777 Caucasian renal cell carcinoma cases and 1,035 controls enrolled in a large European study. Top candidate SNPs were confirmed among 718 Caucasian cases and 615 controls in a second study in the United States. Two of the three SNPs (rs8106822 and rs405509) that replicated in the U.S. study were within a regulatory region of the *APOE* promoter. The ORs for the rs8106822 A>G variant were 1.22_{AG} and 1.41_{GG} in the European study, 1.05_{AG} and 1.51_{GG} in the U.S. study, and 1.15_{AG} and 1.44_{GG} among 1,485 cases and 1,639 controls combined. The rs405509 G>T variant was inversely associated with risk of kidney cancer in the European study (OR = 0.87_{TG}, 0.71_{TT}), the U.S. study (OR = 0.68_{TG}, 0.71_{TT}), and both studies combined (OR = 0.79_{TG}, 0.71_{TT}), as was the G-G haplotype ($r^2 = 0.64$, $p = 4.7 \times 10^{-4}$). This association is biologically plausible because SNP rs405509 was shown to modify protein binding and transcriptional activity of the *APOE* protein *in vitro* and is in linkage disequilibrium with key known variants defining the e2, e3, and e4 alleles that modify risk of atherosclerosis, Alzheimer's disease, and progression of HIV infection to AIDS. (Moore LE, Brennan P, Karami S, Menashe I, Berndt SI, Dong LM, Meisner A, Yeager M, Chanock S, Colt J, Schwartz K, Davis F, Zaridze D, Mattveev V, Janout V, Kollarova H, Bencko V, Navratilova M, Szeszenia-Dabrowska N, Mates D, Holcatova I, Boffetta P, Chow WH, Rosenberg PS, Rothman N. Apolipoprotein E/C1 locus variants modify renal cell carcinoma risk. *Cancer Res* 2009;69:8001–8008)

SARA SCHONFELD SUCCESSFULLY DEFENDS DISSERTATION

In September, Sara Schonfeld, Ph.D., Radiation Epidemiology Branch (REB), successfully defended her doctoral dissertation at the Johns Hopkins Bloomberg School of Public Health. She conducted research for her thesis, "Hormonal factors and the risk of breast and endometrial cancers among postmenopausal nulliparous women," under the mentorship of Dr. Kala Visvanathan of Johns Hopkins; Amy Berrington de Gonzalez, D.Phil. (REB); Patricia Hartge, Sc.D., Epidemiology and Biostatistics Program; Dr. James Lacey, Jr., formerly of the Hormonal and Reproductive Epidemiology Branch; and Ruth M. Pfeiffer, Ph.D., Biostatistics Branch. Dr. Schonfeld will work as a postdoctoral fellow in REB with Elaine Ron, Ph.D., and Ethel S. Gilbert, Ph.D., on studies of radiation dose and cancer mortality in populations affected by activities at the Mayak Nuclear Facility in Russia as well as several other studies in the branch.

Fish, Vitamin D, and Flavonoids

Investigators assessed whether fish, vitamin D, and flavonoid intake affected prospective risk of renal cell cancer among 27,111 male smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study. Among 228 cases, risk (quartile 4 vs. quartile 1) was reduced for the flavonoid quercetin intake (hazard ratio [HR] = 0.6) and increased for Baltic herring intake (HR = 2.0), with adjustment for age, BMI, smoking, blood pressure, alcohol use, physical activity, urban residence, and education. In geographically stratified models, the risks associated with herring and total fish intake appeared to be highest in the urban coast region, although the interaction was not statistically significant. (Wilson RT, Wang J, Chinchilli V, Richie JP, Virtamo J, Moore LE, Albanes D.

Fish, vitamin D, and flavonoids in relation to renal cell cancer among smokers. *Am J Epidemiol* 2009;170:717–729)

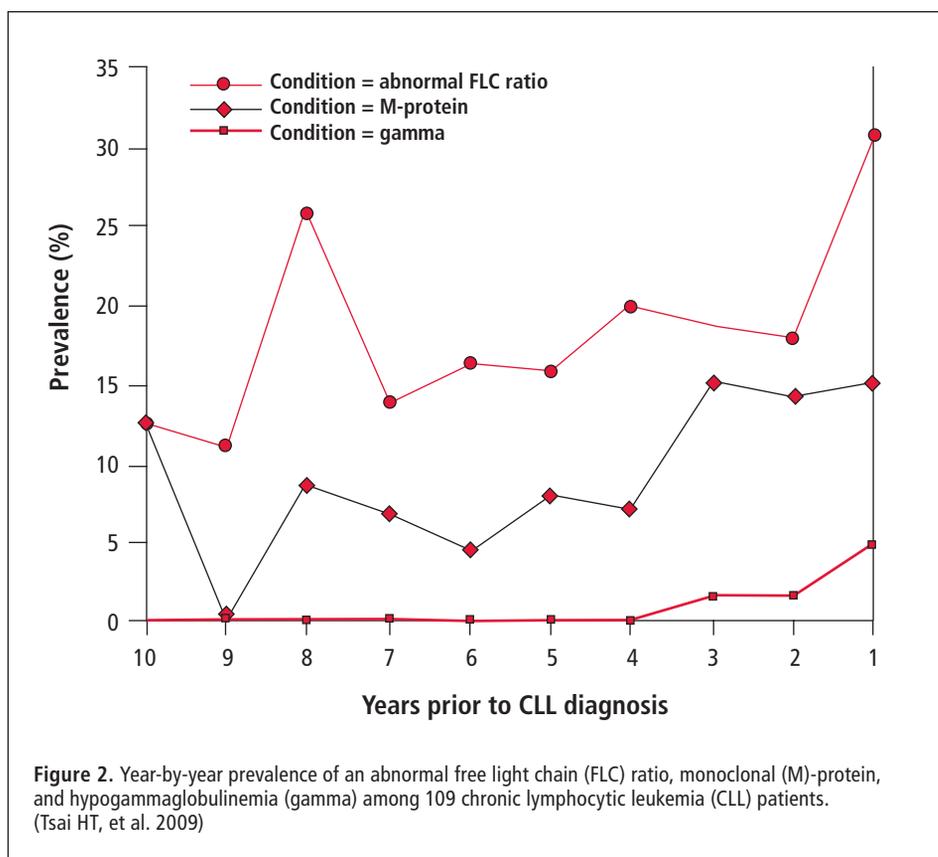


Figure 2. Year-by-year prevalence of an abnormal free light chain (FLC) ratio, monoclonal (M)-protein, and hypogammaglobulinemia (gamma) among 109 chronic lymphocytic leukemia (CLL) patients. (Tsai HT, et al. 2009)

LEUKEMIA

Precursor Immunoglobulin Abnormalities

Among 77,469 participants with serially collected serum samples in the prospective Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, the authors identified 109 persons who developed chronic lymphocytic leukemia (CLL). The authors then evaluated the presence and temporal patterns of monoclonal (M)-proteins, kappa and lambda free light chains (FLCs), and hypogammaglobulinemia in serum from blood obtained up to 9.8 years before CLL diagnosis (see Figure 2). The prevalence of an abnormal FLC ratio, M-protein, and hypogammaglobulinemia before CLL diagnosis was 38%, 13%, and 3%, respectively. M-proteins and abnormal FLC ratios were detected up to 9.8 years before CLL diagnosis in 48 persons (44%). Hypogammaglobulinemia was not present until three years before the diagnosis of CLL. Among 37 patients with information on tumor

cell immunophenotype, an association between immunophenotype and involved FLC ($p = 0.024$, Fisher exact test) was observed. Among 61 persons with a normal FLC ratio and without an M-protein, 17 had elevated kappa or lambda FLC levels, indicating polyclonal B-cell activation. Findings support a role for chronic immune stimulation in CLL genesis. (Tsai HT, Caporaso NE, Kyle RA, Katzmann JA, Dispenzieri A, Hayes RB, Marti GE, Albitar M, Ghia P, Rajkumar SV, Landgren O. Evidence of serum immunoglobulin abnormalities up to 9.8 years before diagnosis of chronic lymphocytic leukemia: A prospective study. *Blood* 2009;114:4928–4932)

LUNG CANCER

GWAS by Histologic Type

The authors conducted a GWAS of lung cancer and its major histologic types, genotyping 515,922 SNPs in 5,739 lung cancer cases and 5,848 controls from one population-based, case-control study and three cohort studies. Results were

combined with summary data from 10 additional studies, for a total of 13,300 cases and 19,666 controls of European descent. Four studies also provided histology data for replication, resulting in 3,333 adenocarcinomas (AD), 2,589 squamous cell carcinomas, and 1,418 small cell carcinomas. In analyses by histology, rs2736100 (*TERT*) on chromosome 5p15.33 was associated with AD risk (OR = 1.23) but not with other histologic types. This finding was confirmed in each replication study and overall meta-analysis (OR = 1.24 for AD). Other previously reported association signals on 15q25 and 6p21 were also refined, but no additional loci reached genome-wide significance. (Landi MT, Chatterjee N, Yu K, Goldin LR, Goldstein AM, Rotunno M, Mirabello L, Jacobs K, Wheeler W, Yeager M, Bergen AW, Li Q, Consonni D, Pesatori AC, Wacholder S, Thun M, Diver R, Oken M, Virtamo J, Albanes D, Wang Z, Burdette L, Doheny KF, Pugh EW, Laurie C, Brennan P, Hung R, Gaborieau V, McKay JD, Lathrop M,

McLaughlin J, Wang Y, Tsao MS, Spitz MR, Wang Y, Krokan H, Vatten L, Skorpen F, Arnesen E, Benhamou S, Bouchard C, Metsapalu A, Voeder T, Nelis M, Vålkk K, Field JK, Chen C, Goodman G, Sulem P, Thorleifsson G, Rafnar T, Eisen T, Sauter W, Rosenberger A, Bickeböller H, Risch A, Chang-Claude J, Wichmann HE, Stefansson K, Houlston R, Amos CI, Fraumeni JF Jr, Savage SA, Bertazzi PA, Tucker MA, Chanock S, Caporaso NE. A genome-wide association study of lung cancer identifies a region of chromosome 5p15 associated with risk for adenocarcinoma. *Am J Hum Genet* 2009;85:679–691

NON-HODGKIN LYMPHOMA

Chronic B-cell Stimulation

To investigate among healthy persons whether serum concentration of soluble CD30 (sCD30), a marker for chronic B-cell stimulation, is associated with non-Hodgkin lymphoma (NHL) risk, a nested case-control study within the PLCO Cancer Screening Trial was conducted. A strong dose-response relationship was found between prediagnostic sCD30 concentration and NHL risk among 234 cases and individually matched controls (OR for second, third, and fourth quartiles vs. first quartile = 1.4, 2.2, 4.1, respectively; $p < 0.001$), which persisted among cases

diagnosed 6–10 years after providing a blood sample. As a similar relationship has been observed among HIV-positive patients, chronic B-cell stimulation may be an important mechanism involved in B-cell lymphomagenesis in both severely immunocompromised and healthy populations. (Purdue MP, Lan Q, Martinez-Maza O, Oken MM, Hocking W, Huang WY, Baris D, Conde B, Rothman N. A prospective study of serum soluble CD30 concentration and risk of non-Hodgkin lymphoma. *Blood* 2009;114:2730–2732)

PANCREATIC CANCER

Smoking-related Risks

Smoking effects were examined in the Pancreatic Cancer Cohort Consortium. When compared with never smokers, current smokers had a significantly elevated risk (OR = 1.77). Risk increased significantly with greater intensity (≥ 30 cigarettes/day: OR = 1.75), duration (≥ 50 years: OR = 2.13), and cumulative smoking dose (≥ 40 pack-years: OR = 1.78). Risk at more than 15 years after smoking cessation was similar to that for never smokers. Estimates of EOR per pack-year declined with increasing intensity, suggesting greater risk for total exposure delivered at lower intensity for longer duration than for higher intensity

for shorter duration. Results suggest that smoking has a late-stage effect on pancreatic carcinogenesis. (Lynch SM, Vrieling A, Lubin JH, Kraft P, Mendelsohn JB, Hartge P, Canzian F, Steplowski E, Arslan AA, Gross M, Helzlsouer K, Jacobs EJ, LaCroix A, Petersen G, Zheng W, Albanes D, Amundadottir L, Bingham SA, Boffetta P, Boutron-Ruault MC, Chanock SJ, Clipp S, Hoover RN, Jacobs K, Johnson KC, Kooperberg C, Luo J, Messina C, Palli D, Patel AV, Riboli E, Shu XO, Rodriguez Suarez L, Thomas G, Tjønneland A, Tobias GS, Tong E, Trichopoulos D, Virtamo J, Ye W, Yu K, Zeleniuch-Jacquette A, Bueno-de-Mesquita HB, Stolzenberg-Solomon RZ. Cigarette smoking and pancreatic cancer: A pooled analysis from the Pancreatic Cancer Cohort Consortium. *Am J Epidemiol* 2009;170:403–413)

PROSTATE CANCER

Insulin, Glucose, and Insulin Resistance

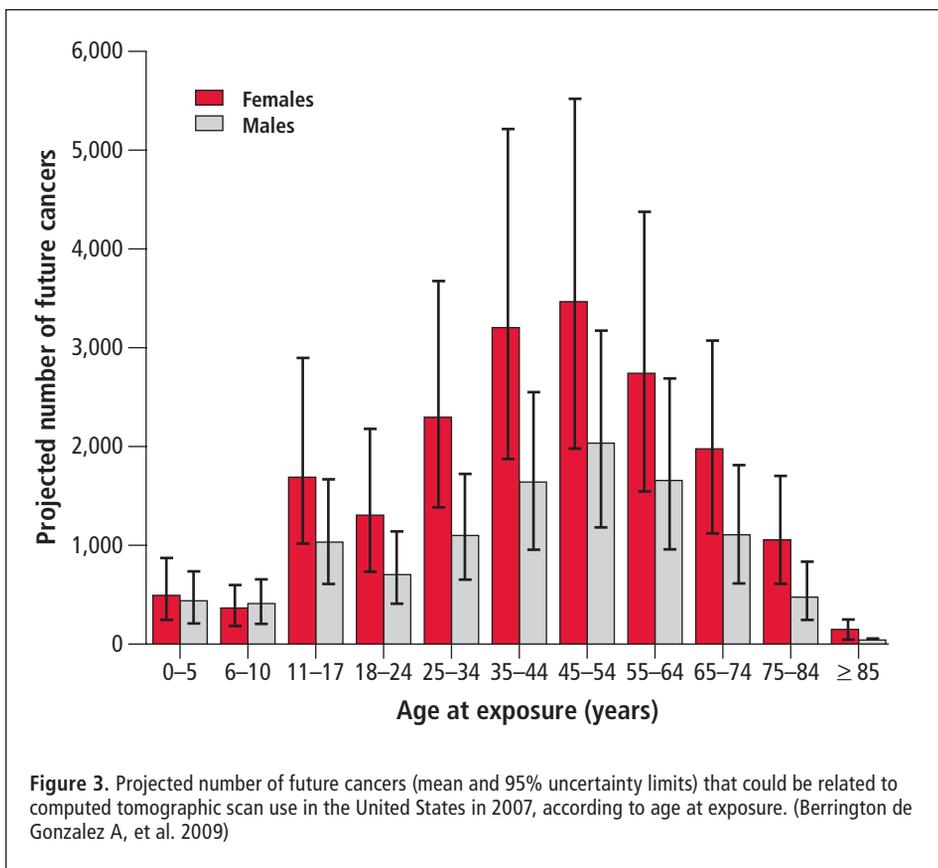
The authors assessed the relationships of levels of serum insulin, glucose, the molar ratio of insulin to glucose, and the homeostasis model assessment of insulin resistance (HOMA-IR) to the development of prostate cancer in a case-cohort study within the ATBC Study cohort of Finnish men. One hundred cases with incident prostate cancer and 400 noncases from the larger cohort were studied. Fasting serum was collected 5–12 years (average 9.2 years) before diagnosis. Insulin concentrations in fasting serum from case subjects were 8% higher than among noncase subjects, and the molar ratio of insulin to glucose and HOMA-IR were 10% and 6% higher in cases, respectively, but these differences were not statistically significant. Compared with insulin levels in the first quartile, those in the second through fourth insulin quartiles were associated with increasing risks of prostate cancer (OR = 1.50, 1.75, and 2.55, respectively; $p = 0.02$). A similar pattern was observed with the HOMA-IR (OR = 2.10, $p = 0.02$) for the highest vs. lowest quartiles.

DYSKERATOSIS CONGENITA WORKSHOP REPORT

The results of the first NIH Clinical Research Workshop on Dyskeratosis Congenita (DC) were reported by **Sharon A. Savage, M.D.**, Clinical Genetics Branch, and colleagues in *Pediatric Blood and Cancer* (2009;53:520–523).

DC is an inherited bone marrow failure syndrome (IBMFS) characterized by very high cancer risks and defects in telomere biology. The workshop was prompted by recent advances in understanding of the genetic defects present in DC and the success of NCI's IBMFS study. The 80 participants included clinicians, scientists, patients with DC, their family members, and representatives from family support groups.

Clinicians and scientists studying DC discussed recent findings, created clinical care recommendations, and developed several new collaborative efforts designed to improve understanding of DC pathogenesis. The patients and family members, numbering 42 participants who represented 17 families, attended a special session that gave them the tools needed to create a family support group. Information on the new group is available at www.dcoutreach.com.



Risk varied inconsistently with glucose concentration. A stronger association between insulin level and prostate cancer risk was observed among leaner men and those who were less physically active at work. (Albanes D, Weinstein SJ, Wright ME, Männistö S, Limburg PJ, Snyder K, Virtamo J. Serum insulin, glucose, indices of insulin resistance, and risk of prostate cancer. *J Natl Cancer Inst* 2009;101:1272–1279)

Meat and Related Compounds

The authors examined the associations between meat consumption (type, cooking method, and related mutagens), heme iron, nitrite/nitrate, and prostate cancer in a cohort of 175,343 U.S. men aged 50–71 years. During 9 years of follow-up, 10,313 prostate cancer cases (1,102 advanced) and 419 fatal cases were ascertained. HRs comparing the fifth intake quintile with the first revealed the following risks associated with red and processed meat for total

(red meat: HR = 1.12, processed meat: HR = 1.07, 95% confidence interval [CI] = 1.00–1.14) and advanced (red meat: HR = 1.31, processed meat: HR = 1.32) prostate cancer. Heme iron, barbecued/grilled meat, and benzo[a]pyrene were all positively associated with total (HR = 1.09, 1.11, and 1.09, respectively) and advanced (HR = 1.28, 1.36, and 1.28, respectively) disease. Nitrite (HR = 1.24) and nitrate (HR = 1.31) intakes were associated with advanced prostate cancer. No clear associations were found for fatal prostate cancer. Red and processed meat may be associated with prostate cancer via mechanisms involving heme iron, nitrite/nitrate, grilling/barbecuing, and benzo[a]pyrene. (Sinha R, Park Y, Graubard BI, Leitzmann MF, Hollenbeck A, Schatzkin A, Cross AJ. Meat and meat-related compounds and risk of prostate cancer in a large prospective cohort study in the United States. *Am J Epidemiol* 2009;170:1165–1177)

Susceptibility Locus on Chromosome 8q24

The authors reported on a GWAS in 10,286 prostate cancer cases and 9,135 controls of European ancestry in the Cancer Genetic Markers of Susceptibility (CGEMS) initiative. The investigators identified a new association with prostate cancer risk on chromosome 8q24 (rs620861, $p = 1.3 \times 10^{-10}$, heterozygote OR = 1.17, homozygote OR = 1.33). This region is of special interest because it is located in a so-called “gene desert” and has been associated with several other forms of cancer. (Yeager M, Chatterjee N, Ciampa J, Jacobs KB, Gonzalez-Bosquet J, Hayes RB, Kraft P, Wacholder S, Orr N, Berndt S, Yu K, Hutchinson A, Wang Z, Amundadottir L, Feigelson HS, Thun MJ, Diver WR, Albanes D, Virtamo J, Weinstein S, Schumacher FR, Cancel-Tassin G, Cussenot O, Valeri A, Andriole GL, Crawford ED, Haiman CA, Henderson B, Kolonel L, Le Marchand L, Siddiq A, Riboli E, Key TJ, Kaaks R, Isaacs W, Isaacs S, Wiley KE, Gronberg H, Wiklund F, Stattin P, Xu J, Zheng SL, Sun J, Vatten LJ, Hveem K, Kumle M, Tucker M, Gerhard DS, Hoover RN, Fraumeni JF Jr, Hunter DJ, Thomas G, Chanock SJ. Identification of a new prostate cancer susceptibility locus on chromosome 8q24. *Nat Genet* 2009;41:1055–1057)

RADIATION

Projected Cancer Risks from Computed Tomographic Scans

The authors generated detailed estimates of future cancer risks from current computed tomographic (CT) scan use in the United States. Risk models based on the National Research Council’s “Biological Effects of Ionizing Radiation” report and organ-specific radiation doses derived from a national survey were used to estimate age-specific cancer risks for each scan type. Models were combined with age- and sex-specific scan frequencies for the United States in 2007 obtained from survey and insurance claims data. The authors estimated that about 29,000

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future cancers could be related to CT scans performed in the United States in 2007. The largest contributions, respectively, were from scans of the abdomen and pelvis, chest, and head and from chest CT angiography. One-third of the projected cancers were due to scans performed at ages 35–54 years, 15% were due to scans performed at ages younger than 18 years, and 66% were in females (see Figure 3). Estimates highlight several areas of CT scan use that make large contributions to the total cancer risk, including several scan types and age groups with a high frequency of use or scans involving relatively high doses, in which risk-reduction efforts may be warranted. (Berrington de Gonzalez A, Mahesh M, Kim KP, Bhargavan M, Lewis R, Mettler F, Land C. Projected cancer risks from CT scans performed in the U.S. in 2007. *Arch Intern Med* 2009;169:2071–2077)

TESTICULAR CANCER

Organochlorine Exposures

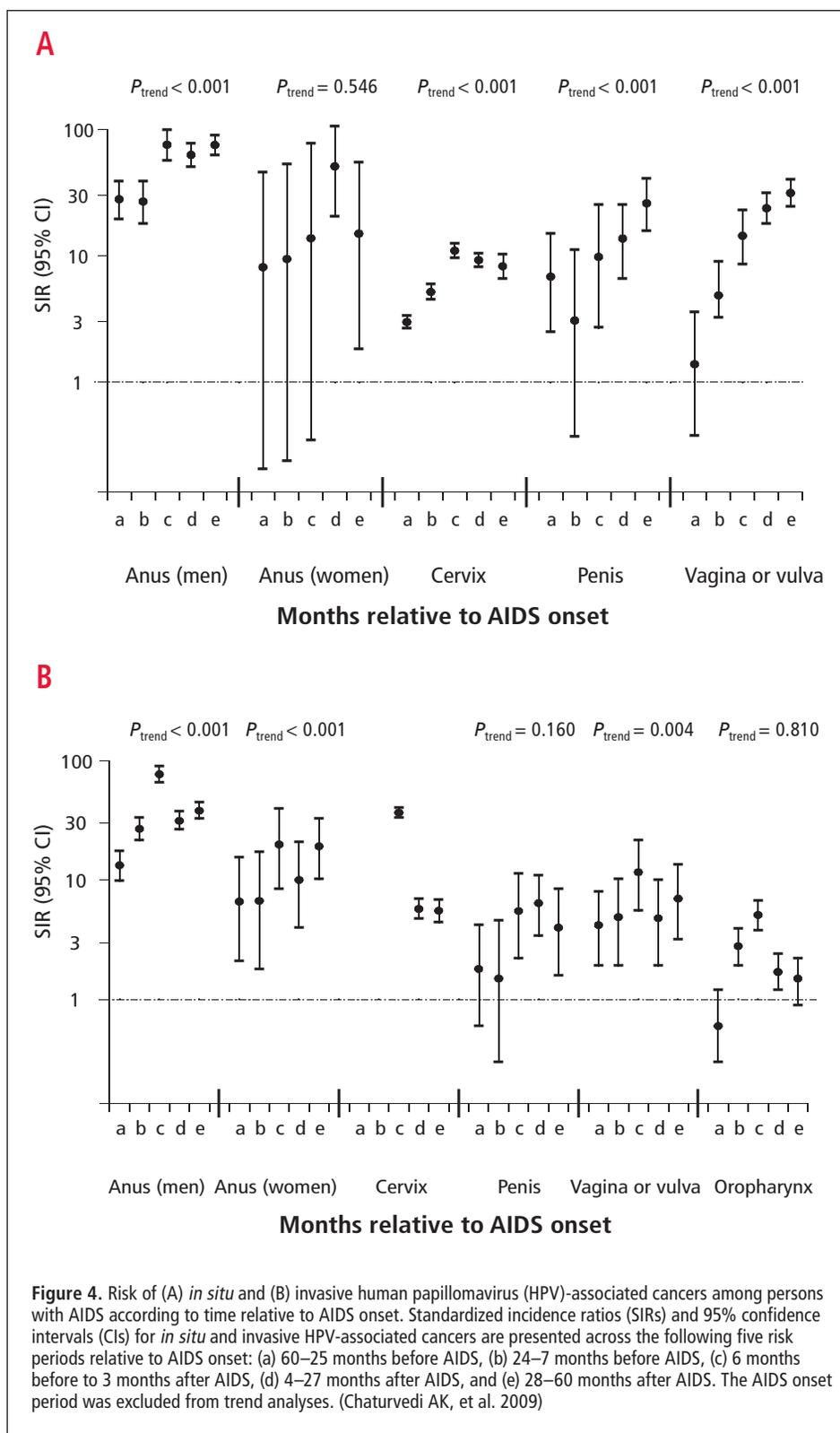
Organochlorine (OC) compounds and the risk of testicular germ cell tumors (TGCTs) were studied in a nested case-control study of TGCTs within the Norwegian Janus Serum Bank cohort among individuals with serum collected between 1972 and 1978. TGCT cases diagnosed through 1999 ($n = 49$) were identified through linkage to the Norwegian Cancer Registry. Controls ($n = 51$) were matched to cases on region, blood draw year, and age at blood draw. TGCT cases had elevated concentrations of p,p' -DDE (tertile 3 vs. tertile 1 OR [OR_{T3}] = 2.2, $p_{\text{Wilcoxon (W)}}$ = 0.07), oxychlorane (OR_{T3} = 3.2, p_{W} = 0.05), *trans*-nonachlor (OR_{T3} = 2.6, p_{W} = 0.07), and total chlordanes (OR_{T3} = 2.0, p_{W} = 0.048) compared with controls, although no ORs were statistically significant. Seminoma cases had significantly lower concentrations of polychlorinated biphenyl (PCB) congeners 44, 49, and 52 and significantly higher concentrations of PCBs 99, 138, 153, 167, 183, and

195. Results provide qualified evidence of an association between TGCT risk and exposures to *p,p'*-DDE, chlordane compounds, and possibly some PCB congeners. (Purdue MP, Engel LS, Langseth H, Needham LL, Andersen A, Barr DB, Blair A, Rothman N, McGlynn KA. Prediagnostic serum concentrations of organochlorine compounds and risk of testicular germ cell tumors. *Environ Health Perspect* 2009;117:1514–1519)

VIRUSES

HPV-associated Cancers in Persons with AIDS

Investigators linked data on 499,230 individuals diagnosed with AIDS from 1980 through 2004 with cancer registries in 15 U.S. regions. Risk of *in situ* and invasive human papillomavirus (HPV)-associated cancers, compared with that in the general population, was measured using standardized incidence ratios (SIRs). The relationship of immunosuppression with incidence 4–60 months after AIDS onset was evaluated by use of CD4 T-cell counts measured at AIDS onset. Incidence 4–60 months after AIDS onset was compared across three periods (1980–1989, 1990–1995, and 1996–2004). Among persons with AIDS, the authors observed elevated risk of all HPV-associated *in situ* (SIRs ranged from 8.9 for cervical cancer to 68.6 for anal cancer among men) and invasive (SIRs ranged from 1.6 for oropharyngeal cancer to 34.6 for anal cancer among men) cancers (see Figure 4). During 1996–2004, low CD4 T-cell count was associated with increased risk of invasive anal cancer among men (RR per decline of 100 CD4 T cells per cubic millimeter = 1.34) and possibly increased risk of *in situ* vaginal or vulvar cancer (RR = 1.52, CI = 0.99–2.35, $p = 0.055$) and invasive cervical cancer (RR = 1.32, CI = 0.96–1.80, $p = 0.077$). Among men, incidence (per 100,000 person-years) of *in situ* and invasive anal cancer was higher during 1996–2004 than during 1990–1995 (29.5



vs. 18.3 *in situ* cases, respectively, RR = 1.71; 42.3 vs. 20.7 invasive cases, respectively, RR = 2.03). Incidence of other cancers was stable over time. (Chaturvedi

AK, Madeleine MM, Biggar RJ, Engels EA. Risk of human papillomavirus-associated cancers among persons with AIDS. *J Natl Cancer Inst* 2009;101:1120–1130)

DCEG PEOPLE IN THE NEWS

In September, **Christian C. Abnet, Ph.D., M.P.H.**, Nutritional Epidemiology Branch (NEB), gave a keynote speech titled “Epidemiologic studies of esophageal cancer: Out of the lab and into people” at the University of Pittsburgh Department of Biological Science Annual Retreat in Pymatuning, Pennsylvania.

In December, **Demetrius Albanes, M.D.** (NEB), chaired a plenary session titled “Current controversies in nutritional epidemiology and cancer chemoprevention” and gave a presentation on

“Beta-carotene chemoprevention trials and lessons for cancer epidemiology and prevention” at the American Association for Cancer Research’s Frontiers in Cancer Prevention Research Conference in Houston, Texas.

In October, **Amy Berrington de Gonzalez, D.Phil.**, Radiation Epidemiology Branch (REB), gave an invited talk on late health effects in irradiated populations at the Annual Meeting of the Radiation Research Society in Savannah, Georgia.

In October, **Louise A. Brinton, Ph.D.**, Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), gave a presentation titled “Cancer risk among infertile women with androgen excess or menstrual disorders (including polycystic ovary syndrome)” at the American Society for Reproductive Medicine’s 65th Annual Meeting in Atlanta, Georgia.

In November, **Neil E. Caporaso, M.D.**, Genetic Epidemiology Branch (GEB), and Dr. Stefan Ambs of the Center for Cancer Research co-led a session on health disparities and epidemiology during the Translational Research in Clinical Oncology Course on the NIH campus in Bethesda, Maryland.

MARK SCHIFFMAN WINS AACR-PREVENT CANCER FOUNDATION AWARD

In December, **Mark Schiffman, M.D., M.P.H.**, Clinical Genetics Branch, attended the 8th Annual International Conference on Frontiers in Cancer Prevention Research in Houston, Texas, where he received the American Association for Cancer Research (AACR)-Prevent Cancer Foundation Award for Excellence in Cancer Prevention Research and presented a lecture titled “Biomarkers and cancer prevention: Cautionary lessons from the study of human papillomavirus and cervical cancer.”

The AACR-Prevent Cancer Foundation Award for Excellence in Cancer Prevention Research is given annually to a scientist residing in any country in the world for his or her contributions to the field of cancer prevention. The scientist’s investigations must have been conducted in basic, translational, clinical, epidemiological, or behavioral science in cancer prevention research. Furthermore, these studies must have not only had a major impact on the field but also stimulated new directions in this important area.

Dr. Schiffman was chosen by peer review for his outstanding research on human papillomavirus infection and cervical carcinogenesis. The presenters noted that his work has changed cervical cancer screening and prevention in the United States and internationally. The award cites Dr. Schiffman’s research as a model of interdisciplinary science involving collaborations between molecular biologists, virologists, geneticists, vaccinologists, diagnosticians, clinicians, epidemiologists, and public health scientists and notes the combination of etiologic and preventive impact.



Mark Schiffman

In December, **Carrie R. Daniel, Ph.D., M.P.H.** (NEB), gave two talks—“Dietary patterns and scores for pooled analyses with body-size and mortality” and “Preliminary analysis and collaborative proposal to the Diet Working Group of the ACC”—at the Asian Cohort Consortium (ACC) meeting in Tokyo, Japan.

In November, **Sanford M. Dawsey, M.D.** (NEB), gave invited talks on “PAH exposure—A universal risk factor for esophageal squamous cell carcinoma?” at the Cancer Council New South Wales in Sydney, Australia and on “Esophageal squamous cell carcinoma: The other esophageal cancer” at the Queensland Institute of Medical Research in Brisbane, Australia.

Eric A. Engels, M.D., M.P.H., Infections and Immunoepidemiology Branch (IIB), spoke in August on “Epidemiology of thymic malignancies” at the First International Conference on Thymic Malignancies at NIH in Bethesda, Maryland and in November on “Epidemiology

of cancer in HIV-infected people” at the American Society of Cytopathology Meeting in Denver, Colorado.

In October, **Alisa M. Goldstein, Ph.D.** (GEB), was the Scientific Program Chair for the 18th Annual Meeting of the International Genetic Epidemiology Society in Kahuku, Hawaii.

In November, **Mark H. Greene, M.D.**, Chief of the Clinical Genetics Branch, presented “GOG-199 status report and a glimpse into the future of ovarian cancer screening” at the Society of Gynecologic Oncologists’ State of the Art Conference on Personalized Gynecologic Care in Washington, DC.

During a special session titled “Hematopoietic and lymphoid neoplasms” at the Surveillance, Epidemiology, and End Results (SEER) Principal Investigator Retreat, **Ruth A. Kleinerman, M.P.H.**, and **Lindsay M. Morton, Ph.D.**, both of REB, gave a joint invited talk on “Evolving classification of lymphoma: Relevance for epidemiologic research.” They spoke on the same topic at the Beebe Symposium in November in Washington, DC. During that same month, Ms. Kleinerman presented a poster on “Risk of second cancers following treatment for retinoblastoma since 1970” and Dr. Morton presented a poster on “Immunostaining for CD10, BCL6, MUM1, LMO2, and BCL2 to identify favorable survival for molecular subtypes of diffuse large B-cell lymphoma in a population-based study during the pre-rituximab era” at the NCI Translational Science Meeting in Vienna, Virginia.

In December, **Shih-Wen (Wenny) Lin, Ph.D., M.P.H.** (NEB), received a Scholar-in-Training Award to attend the American Association for Cancer Research meeting Frontiers in Cancer

Prevention Research in Houston, Texas and present her poster on “Alcohol consumption and TMRSS2: ERG gene fusion in prostate cancer.”

In October, **Thomas R. O’Brien, M.D., M.P.H.** (IIB), spoke on “IL-28B predicts IFN response with hepatitis C” at the Perspectives in Melanoma XIII Meeting in Baltimore, Maryland.

In December, **Preetha Rajaraman, Ph.D.** (REB), gave an invited talk titled “Cancer risk after medical exposure: Second malignancies after childhood cancer in the Childhood Cancer Survivor Study (CCSS)” at the National Institute of Radiological Sciences in Chiba, Japan.

In October, **Arthur Schatzkin, M.D., Dr.P.H.**, Chief of NEB, presented “A new partnership in biomedical and lifestyle research: The NIH-AARP Diet and Health Study” at the AARP Annual Meeting in Las Vegas, Nevada.

In September, **Mark E. Sherman, M.D.** (HREB), gave a lecture on “Etiologic heterogeneity in breast cancer: Pathway to prevention or road to ruin?” at Strangeways Research Laboratory at the University of Cambridge, United Kingdom. During the same month, Dr. Sherman and **Gretchen L. Gierach, Ph.D.** (HREB), gave a joint presentation titled “Mammographic density and breast cancer risk” at the Barbara Ann Karmanos Cancer Institute in Detroit, Michigan.

UGANDAN DELEGATION VISITS DCEG

In October, **Sam M. Mbulaiteye, M.D.**, Infections and Immunoepidemiology Branch, hosted five scientists from Uganda during a three-day visit to DCEG. The scientists met with members of DCEG, Information Management Services, Inc., and RTI International, Inc., to plan the fieldwork of a new collaborative study, East Africa Epidemiology of Burkitt Lymphoma in East African Children and Minors (EMBLEM). The Ugandan delegation promised to send the Division a Ugandan flag when the first child with Burkitt lymphoma is enrolled in the study, which is scheduled for early this year.



Ugandan Delegation at DCEG: (front) Joseph Fraumeni and Sam Mbulaiteye; (back) Patrick Kerchan, Allan Hildesheim, Mike Mbaziira, Tobias Kinyera, Olivia Namusisi, James Goedert, and Martin Ogwang.

Meredith Shiels, Ph.D., and **Edgar Simard, M.P.H.**, both of IIB, received Young Investigator Awards to attend the Conference on Retroviruses and Opportunistic Infections in San Francisco, California in February.

Rashmi Sinha, Ph.D. (NEB), gave talks on meat and meat-related carcinogens at the Harvard School of Public Health in Boston, Massachusetts; the University of Arkansas for Medical Sciences in Little Rock, Arkansas; and the National Cancer Center in Tokyo, Japan. She also spoke on “ASA24, a self-administered instrument for collecting 24-hour dietary recall information” and chaired a session on the Dietary Pattern Working Group at the Asian Cohort Consortium Meeting in Tokyo, Japan.

Rachael Stolzenberg-Solomon, Ph.D., M.P.H., R.D. (NEB), gave invited talks on pancreatic cancer in October at the Prevention Grand Rounds at Roswell Park Cancer Institute in Buffalo, New York; in November at the Lunch-LearnLink, Maryland Cigarette Restitution Fund Program, Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland; and in December



Julia Ciampa

In November, **Julia Ciampa, M.Sc.**, Biostatistics Branch, won an NIH Graduate Student Research Award for her poster on “Derivation, evaluation, and application of a novel multilocus method for genome-wide association studies: Implications for oncogenic potential of 8q24,” presented at the 10th NIH Graduate Student Research Symposium in Bethesda, Maryland. Winners receive a \$1,000 travel award from the NIH Graduate Partnership Program office.

at Imperial College London in the United Kingdom and as key speaker at a Pancreatic and Colorectal Cancer Minisymposium at the University Medical Center Utrecht in The Netherlands.

Philip R. Taylor, M.D., Sc.D. (GEB), spoke on “Micronutrients for the prevention of cancer: A success story” at the Office of Dietary Supplements Fall Seminar Series at NIH in Bethesda, Maryland in October and at the Cancer Council New South Wales Research Strategy and Scientific Development Unit in Sydney, Australia in November. He also presented “Upper gastrointestinal cancer genetic studies” at the InterSCOPE meeting at the Cancer Council New South Wales in Sydney, Australia in November and taught “Chemoprevention of cancer”

at the Fundamentals of Oncology for Public Health Practitioners course at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland in December.

At the Society for Melanoma Research International Congress in Boston, Massachusetts in November, **Margaret A. Tucker, M.D.**, Director of the Human Genetics Program and Chief of GEB, gave a talk on “UV melanoma risk” and **Maria Teresa Landi, M.D., Ph.D.** (GEB), chaired the Melanoma Epidemiology Session and spoke on “Current knowledge and challenges in the epidemiology of melanoma.”

In January, **Nicolas Wentzensen, M.D., Ph.D.** (HREB), gave an invited presentation on “Screening test options: Current practice and future developments” at the Workshop for Cervical Cancer Prevention along the U.S.-Mexico Border in Albuquerque, New Mexico.

In December, **Regina G. Ziegler, Ph.D., M.P.H.**, Epidemiology and Biostatistics Program, presented “A new approach to measuring steroid hormone exposure and metabolism in epidemiologic studies” at Harvard Medical School in Boston, Massachusetts.

NEW FELCOM REPRESENTATIVES

Mercy Guech-Ongey, Ph.D., Infections and Immunoepidemiology Branch, and **Gila Neta, Ph.D.**, Radiation Epidemiology Branch (REB), have been appointed to represent DCEG on the NIH Fellows Committee, also known as FelCom. They are replacing outgoing members **Porcia Bradford, M.D.**, Genetic Epidemiology Branch, and **Chu-Ling Yu, Sc.D.** (REB). FelCom enhances communication among fellows and the NIH community and serves as a liaison to leaders of programs that affect the training experience. More information about FelCom is available at <http://felcom.od.nih.gov>.



New FelCom Representatives: Mercy Guech-Ongey and Gila Neta.

COMINGS . . . GOINGS



Amanda Black

Amanda Black, Ph.D., M.P.H., joined the Epidemiology and Biostatistics Program as a staff scientist to work on the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. She previously was a Cancer Prevention Fellow with the Early Detection Research Network in the Division of Cancer Prevention. She received a B.Sc. in biomedical science, an M.Sc. in medical laboratory science, a Ph.D. in epidemiology and public health from Queen's University in Belfast, and an M.P.H. from the University of Manchester. Her research interests include early detection, screening, and disease etiology with particular focus on prostate and ovarian cancer.



David Capo-Ramos

David Capo-Ramos, M.D., M.P.H., joined the Genetic Epidemiology Branch as a research fellow. He received an M.D. in 2007 and an M.P.H. in 2009 from the University of Puerto Rico. For his master's dissertation, he examined the role of particulate matter emissions in asthma and other respiratory diseases among residents of two areas of Puerto Rico. Dr. Capo-Ramos is working with **Maria Teresa Landi, M.D., Ph.D.**, on the etiology and progression of lung cancer.



Sharon Coles-Calloway

Sharon Coles-Calloway joined DCEG's Administrative Resource Center (ARC) as the lead purchasing agent. She has worked as a purchasing agent at NCI for

the past 10 years, providing procurement support to the Urologic Oncology Branch, Metabolism Branch, and Surgery Branch of the Center for Cancer Research. Ms. Coles-Calloway brings with her a wealth of experience and a can-do attitude. Before becoming a purchasing agent, she held administrative support positions with the U.S. Office of Personnel Management and the U.S. Department of Commerce.



Cher Dallal

Cher Dallal, Ph.D., joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a Cancer Prevention Fellow. She has a B.A. in molecular and cell biology from the University of California, Berkeley; an M.P.H. from Yale University; an M.S. in applied biostatistics and epidemiology from the University of Southern California; and a Ph.D. in epidemiology from the University of Pittsburgh. In her doctoral dissertation, Dr. Dallal evaluated the relationship of estrogen metabolites to breast cancer risk. At DCEG, she is working with **Louise A. Brinton, Ph.D.**, Chief of HREB, and **Gretchen L. Gierach, Ph.D.**, to assess

the relationships of hormones to endometrial and breast cancer risk in the Fracture Intervention Trial Follow-up Study and to evaluate physical activity as determined by accelerometer measurements in the Polish Breast Cancer Study.



Sonja Dawsey

Sonja Dawsey joined the Nutritional Epidemiology Branch (NEB) as a Cancer Research Training Award predoctoral fellow. She received a B.S. in cellular and molecular biology from the University of Michigan in Ann Arbor, Michigan. She is working with **Christian C. Abnet, Ph.D., M.P.H.**, on esophageal cancer studies in Kenya.



Benjamin Emmanuel

Benjamin Emmanuel joined the Infections and Immunoepidemiology Branch (IIB) as a special volunteer. He received a B.S. in biology from Wheaton College in Illinois and is completing an M.P.H. at George Washington University. He is working with **Sam M. Mbulaiteye, M.D.**, on Burkitt lymphoma studies in Africa.

DENISE STONEMAN RETIRES

Denise Stoneman started her career at NIH in 1978 as a secretary for the deputy director of the National Institute of Allergy and Infectious Diseases (NIAID). After spending 10 years at NIAID, she joined NCI as a grants technical assistant in the Division of Extramural Activities. She began working as a program assistant under Dr. Alan Rabson, NCI Deputy Director, in 1989 and was later promoted to administrative officer for MaryAnn Guerra, NCI's Deputy Director for Management, in the Building 31 Administrative Resource Center (ARC). In 1998, Ms. Stoneman moved to the DCEG ARC, where she provided service to the Occupational and Environmental Epidemiology Branch, the Radiation Epidemiology Branch, and the Biostatistics Branch. She has been an invaluable asset to the ARC and the Division. Using her expertise and knowledge in the administrative and budget areas, she has trained many junior staff at the ARC, enabling them to obtain higher-level positions within NCI. After her retirement, Ms. Stoneman moved with her husband to a farm in North Carolina, where she plans to enjoy the great outdoors, running, hiking, riding horses, and kayaking.



Jacqueline Feenster

Jacqueline Feenster

joined the Office of Division Operations and Analysis (ODOA) as a scientific program specialist. She is working on data compilation and analysis for reporting and budget activities and is maintaining systems and databases used by DCEG and NIH. Previously, she was a protocol management specialist in the NIH Clinical Center's Rehabilitation Medicine Department and the NCI Protocol and Information Office as well as a senior research coordinator for Johns Hopkins University. She received a B.S. from the University of Maryland, Eastern Shore.

Roberto Flores, Ph.D., M.P.H., joined IIB as a Cancer Prevention Fellow. He has a Ph.D. in nutritional sciences from the University of Arizona in Tucson and an M.P.H. from the Johns Hopkins



Roberto Flores

Bloomberg School of Public Health. He previously worked as a laboratory scientist directing a human papillomavirus (HPV) molecular screening

laboratory and developing and validating high-throughput real-time polymerase chain reaction assays for the absolute quantification of eight oncogenic HPV types. During his public health training, he evaluated national HPV vaccine implementation and cervical cancer screening programs in India. He is working with **James J. Goedert, M.D.,** on research related to the association of the gut microbiome to cancer.

Jecholia Gallagher joined ODOA as a scientific program specialist. She received a B.A. from George Mason University in Fairfax, Virginia. She is working on data compilation and analysis for reporting



Jecholia Gallagher

and budget activities and is maintaining systems and databases used by DCEG and NIH. Previously, she worked at Global Solutions Network, Inc., and Ariel Research/3E Company, where she was the regulatory services coordinator and served on the integrative content team compiling and integrating chemical regulation information.



Choonsik Lee

Choonsik Lee, Ph.D., joined the Radiation Epidemiology Branch (REB) as a tenure-track investigator. He completed his Ph.D. in health physics at

Hanyang University and postdoctoral fellowships in health physics and medical physics at the Innovative Technology Center for Radiation Safety in Korea and the University of Florida, respectively. His interests include human computational models, called hybrid phantoms. At REB, he is building the first comprehensive organ dose database for pediatric and adult patients from computed tomography and radiography examinations as well as analyzing organ doses from external radiation treatment using Monte Carlo simulation.



Wenny Lin

Shih-Wen (Wenny) Lin, Ph.D., M.P.H.,

joined NEB as a Cancer Prevention Fellow. She has a B.S. in biochemistry from the University of Dela-

ware, a Ph.D. in cell and molecular biology from the University of Pennsylvania, and an M.P.H. from the Harvard School of Public Health. For her doctoral dissertation, she worked with Dr. Hildeg HIV-1-specific adaptive immune responses elicited by prime-boost regimens using adenovirus and adeno-associated virus vectors as vaccine



B.J. Stone

B.J. STONE RETIRES

Betty Jane (B.J.) Stone, Ph.D., Biostatistics Branch (BB), retired in December after a 34-year career at DCEG. She joined the Division in 1975 as a part-time guest worker, offering her computer skills in exchange for on-the-job training in epidemiology. Six months later, she was hired full-time as a cancer expert, and she spent the remainder of her career in the Division.

Dr. Stone received a B.S. with honors from Swarthmore College and a Ph.D. from Stanford University, both in mathematics. Before joining NCI, she built mathematical models for research institutes and in private industry, and she also taught for two years at Harvey Mudd College.

During her career at NCI, Dr. Stone provided statistical analysis and computer support to epidemiologists throughout the Division and coauthored several reports investigating geographic "hot spots" of cancer mortality identified from U.S. county-based maps. She was a scientific editor of monographs, research articles, and site visit reports—a role especially important to foreign-born scientists, many of whom benefited greatly from her superb editorial skills. Dr. Stone chaired the Technical Evaluation of Questionnaires Committee for more than 20 years and developed the Questionnaire Modules web site, a searchable collection of questionnaire modules that has proven useful to scientists who are developing questionnaires for new studies. She also served as an administrator of the NCI Cancer Genome Atlas web site.

Dr. Stone was a singer and orchestra manager for Washington, DC's Friday Morning Music Club Chorale for two decades and was a member of the DCEG chorus. For many years, she recorded scientific texts for Recording for the Blind & Dyslexic. A regular blood donor at the NIH Blood Bank, she donated more than 15 gallons of blood over the years. Following her retirement, Dr. Stone moved to Carlsbad, California, where she plans to enjoy the weather and many activities. She will continue to provide scientific editing services to BB as a part-time contractor.

carriers. During her public health training, Dr. Lin explored the relationship of alcohol consumption to prostate cancer and of caffeine consumption to preterm birth. She is working with **Christian C. Abnet, Ph.D., M.P.H.**, on the etiology of esophageal and stomach cancer.



Jacqueline Major

Jacqueline Major, Ph.D., joined NEB as a postdoctoral fellow. She has an M.S. in statistics from San Diego State University and a Ph.D. in epidemiology from the University of California, San Diego (UCSD). For her doctoral dissertation, she worked with Dr. Hillary Klonoff-Cohen and Dr. Dan Mercola to examine body mass in relation to pathological, clinical, and genetic components of prostate cancer progression in men who underwent radical prostatectomy. She also worked with Dr. Elizabeth Barrett-Connor on the Rancho Bernardo Study to examine circulating insulin-like growth factor 1 (IGF-I) and subsequent cancer mortality. Before pursuing her doctorate, she was a senior statistician at UCSD Moores Cancer Center. Dr. Major is studying the etiology of prostate and other cancers, including the roles of growth factors, vitamins, trace elements, and genetic variants, with **Demetrius Albanes, M.D.** She is also working on novel statistical approaches to nutritional epidemiological analysis with **Barry I. Graubard, Ph.D.**; **Arthur Schatzkin, M.D., Dr.P.H.**, Chief of NEB; and **Rashmi Sinha, Ph.D.**

Charles E. Matthews, Ph.D., has joined NEB as a physical activity epidemiologist. He received a B.S. in exercise science and a Ph.D. in epidemiology from the University of Massachusetts and an M.S. in exercise science from the University of South Carolina. He previously worked in the Department of Epidemiology and Biostatistics at the University of South Carolina and at the



Charles Matthews

Saloni Nayar joined the DCEG Office of Communications and Special Initiatives as an NCI Health Communications Intern. She will graduate with an M.P.H. from the University of Iowa this May.



Sarah Nyante

Sarah Nyante, Ph.D., joined HREB as a postdoctoral fellow. She received a B.S. in molecular, cellular, and developmental biology from Yale University and an M.S.P.H. and Ph.D. in epidemiology from the University of North Carolina at Chapel Hill. For her doctoral dissertation, she worked with Dr. Robert Millikan to assess the relationships between single nucleotide polymorphisms and basal-like and luminal A breast cancers in the Carolina Breast Cancer Study. She is focusing on the etiologic heterogeneity of breast and gynecologic cancers.

Scott Quinlan, M.S., a predoctoral fellow with IIB, has left to take a position as a senior analyst at HealthCore in Wilmington, Delaware.

Elizabeth Hill Ruder, Ph.D., M.P.H., R.D., joined NEB as a Cancer Prevention Fellow. She has a B.S. in nutrition science from Cornell University, an M.P.H. from the Johns Hopkins Bloomberg School of Public Health, and a Ph.D. in nutrition science from Pennsylvania State University. A registered dietitian, she completed internship training at the Cleveland Clinic Foundation. For her doctoral dissertation, she worked with

Vanderbilt University School of Medicine. His research program is designed to discover how to prevent and control cancer through etiologic and methodological studies of physical activity behaviors in the population.



Elizabeth Ruder

Dr. Terry Hartman of Penn State and Dr. Joanne Dorgan of Fox Chase Cancer Center to assess the relationship of birth characteristics to age at menarche and concentrations of serum sex hormones during adolescence. At NEB, she is working with **Amanda J. Cross, Ph.D.**, and **Rashmi Sinha, Ph.D.**, to assess diet-related risk factors for colorectal cancer.



David Wheeler

David Wheeler, Ph.D., M.P.H., joined the Occupational and Environmental Epidemiology Branch as a Cancer Prevention Fellow. He holds an M.S. in applied statistics and a Ph.D. in geography, with a specialization in spatial statistics, from Ohio State University and an M.P.H. from Harvard University. His previous research includes applying statistical methods to investigate childhood cancer clusters and modeling ethnic disparities in disease with hierarchical Bayesian models. With his mentor, **Mary H. Ward, Ph.D.**, he is working on multiple projects involving spatial analysis of cancer incidence and mortality data with a focus on lymphohematopoietic tumors in adults and children.



Jessica Wilcox

Jessica Wilcox was promoted to administrative officer in ARC. She is providing administrative and budget support to REB. Previously, she worked as an administrative technician in the ARC for three years, supporting the work of three senior administrative officers. She has many years of administrative experience and is committed to the mission of the ARC and DCEG.

CELEBRATING 30 YEARS OF CANCER RESEARCH WITH CHINA

In November, NCI and the Chinese Academy of Medical Sciences (CAMS) co-sponsored the workshop “Personalized cancer medicine: Building on thirty years of China-U.S. scientific progress,” which was held in Beijing to celebrate and foster collaborative cancer research. The meeting, chaired by Dr. Anna Barker, NCI Deputy Director, and Dr. Qimin Zhan, Vice President of CAMS, was attended by more than 100 scientists, including John Niederhuber, M.D., NCI Director.

Several presentations by DCEG investigators, Division alumni, and long-time collaborators recognized and illustrated DCEG’s efforts in the long-standing collaborative research program. **Ann W. Hsing, Ph.D.**, Hormonal and Reproductive Epidemiology Branch, discussed a multidisciplinary, population-based study conducted by DCEG and the Shanghai Cancer Institute (SCI) on biliary tract cancer, which is rising sharply in incidence in China. **Qing Lan, M.D., Ph.D., M.P.H.**, Occupational and Environmental Epidemiology

Branch, described collaborative work with the Chinese Center for Disease Control and Prevention that examined the relation of occupational benzene exposure to acute myeloid leukemia, aplastic anemia, and other hematopoietic disorders. **Philip R. Taylor, M.D., Sc.D.**, Genetic Epidemiology Branch, reported on a clinical trial evaluating the effects of nutrient supplementation on esophageal cancer mortality in a high-risk population.

Dr. Wei Zheng, professor and Chief of the Division of Epidemiology at Vanderbilt University, spoke on early results from the Shanghai Women’s Health Study. Dr. Wei-Cheng You, President of the Beijing Cancer Hospital at Peking University, described an intervention trial that tested the effect of anti-Helicobacter therapy and a COX-2 inhibitor on precursor lesions to gastric cancer. Both Drs. Zheng and You are DCEG alumni. Dr. Yu-Tang Gao, former Director of SCI, summarized several SCI–DCEG



DCEG Presenters: Ann Hsing, Philip Taylor, and Qing Lan.

collaborations, including a case-control study of lung cancer in non-smoking women. Other presentations by U.S. and Chinese scientists focused on genomics, epigenomics, the next generation of sequencing, and their impact on cancer prevention and treatment. The meeting closed with a consensus that U.S.–China collaborations will become increasingly important in accelerating progress toward personalized cancer medicine on a global scale. ■

—Ann W. Hsing, Ph.D.



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