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New Malignancies Among Cancer Survivors

Compared with the general population, survivors of certain forms of cancer have an increased risk of developing a subsequent primary cancer, according to a new monograph published by DCEG in collaboration with the Division of Cancer Control and Population Sciences. In many cases, the patterns of excess risks that emerged suggested the effect of risk factors shared by the primary and subsequent cancers, whereas some cases suggested a carcinogenic effect of cancer therapies.

The monograph, entitled *New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973–2000,* is the first to provide a comprehensive analysis of the risk of developing a new malignancy in the U.S. population. "A number of studies have evaluated the risk of subsequent tumors following particular forms of cancer, often related to the late effects of treatment, but this report systematically evaluates subsequent cancer risk for all common and uncommon forms of cancer," said **Rochelle E. Curtis, M.A.,** a statistician in the Radiation Epidemiology Branch and the monograph's lead editor.

The report used data from nine cancer registries participating in the Surveillance, Epidemiology, and End Results (SEER) Program from 1973 to 2000. A key

Lead Editors of Monograph: D. Michal Freedman, Elaine Ron, Rochelle Curtis, Lynn Ries, Joseph Fraumeni, David Hacker, Brenda Edwards, and Margaret Tucker.

DCEG *Linkage*

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feature of these registries is that they are population-based and report on cancer incidence for approximately 10 percent of the U.S. population. The SEER Program has set the standard for high quality and completeness of data for cancer registries around the world.

"The monograph is by far the largest study to date to assess risk of subsequent cancers and covers more than 2 million cancer survivors during a nearly 30-year period and more than 185,000 subsequent primary cancers," said **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG and senior editor of the monograph.

More than 50 adult and 18 childhood cancers are included in the new report, including new data on less common cancer sites. More than 350 data tables present the risk of subsequent cancer by time since initial diagnosis, gender, age at initial diagnosis, and when appropriate, by treatment and histologic type. Each chapter focuses on a specific initial cancer, presents the risks of second cancers, and discusses potential causal mechanisms. "The monograph provides a resource that will be useful to clinicians, researchers, policy makers, and cancer survivors, especially in tailoring appropriate guidelines and strategies for prevention and early detection of new malignancies," Dr. Fraumeni said.

"The study of multiple primary cancers has expanded greatly since the early 1980s," explained **Margaret A. Tucker, M.D.,** Director of DCEG's Human Genetics Program and a monograph coeditor. "During this period, survival has improved dramatically due to advances in the treatment of cancer and its detection at an early stage." Over the last few decades, five-year relative survival rates in the United States have increased steadily to 66 percent among adults and 79 percent in children, so about 10.5 million people in the United States were living with cancer as of January 1, 2003. For some, however, the improvements in survival have come at a cost in the form of long-term consequences of the disease and its treatment, including a heightened risk of a new primary cancer.

In the overall analysis, cancer survivors from SEER data had a 14 percent higher risk of developing a subsequent cancer than would be expected in the general population, after taking age, sex, race, and calendar year of follow-up into account. A total of 185,407 new malignancies were observed (O), compared with 162,602 cancers expected (E), giving an observed-to-expected ratio (O/E) of 1.14 (95% confidence interval = 1.14–1.15). Females had a slightly higher relative risk than males for all subsequent cancers combined (O/E = 1.17 for females vs. 1.11 for males), but the difference was mainly due to sex-specific cancers, such as female breast and prostate.

The risk of new cancers also varied by age, with an O/E ratio more than six-fold for survivors of childhood cancer (aged < 18 years). A total of 352 subsequent cancers were observed following childhood tumors, compared with only 58 cancers expected, with patterns suggesting an effect of cancer therapy and genetic susceptibility. The risks were also increased about two- to threefold among those whose first cancers were diagnosed as young adults (aged 18 to 39 years).

In addition to providing estimates of the relative risk in the form of O/E ratios, the monograph evaluated the excess absolute risk (EAR) of new malignancies for each cancer site. Among all cancer survivors combined, the EAR was estimated at 21 excess cancer cases per 10,000 person-years. The greatest burden of subsequent

cancers was among patients initially diagnosed at ages 30 to 59 years, with EARs ranging from 32 to 39 per 10,000 person-years at risk for all initial malignancies combined. The absolute risk of developing a new malignancy was relatively low for children (EAR = 15) because most have not yet reached the ages of higher cancer incidence rates.

"It will be especially important to continue surveillance for late-occurring subsequent cancers as survivors enter the period of life when background cancer rates increase substantially," Ms. Curtis said. Figure 1 shows the trend in risk over time, with nearly 14 percent of SEER patients developing a second cancer in 25 years of follow-up.

A sizable portion of multiple cancers in the SEER database represented multicentric tumors that occurred in the same or neighboring organ system, but most of the subsequent cancers occurred in diverse sites. Many of the patterns of multiple cancers in the monograph suggested an effort of shared risk factors. Of particular importance were tobacco and alcohol consumption, but nutritional factors (e.g., obesity), hormones, infections and immunosuppression, and genetic predisposition also played a role. Ms. Curtis emphasized that "tobacco- and alcohol-related cancer sites accounted for more than 35 percent of the excess cancers occurring in this survey. The EAR for these survivors was particularly high, at 114 excess cancers per 10,000 person-years."

"The oncology community has been quite concerned that certain cancer treatments may lead to an elevated risk of second cancers," Dr. Tucker said. The overall data from the monograph indicated that children and young adults seemed especially prone to the carcinogenic effects of intensive radiotherapy and chemotherapy regimens.

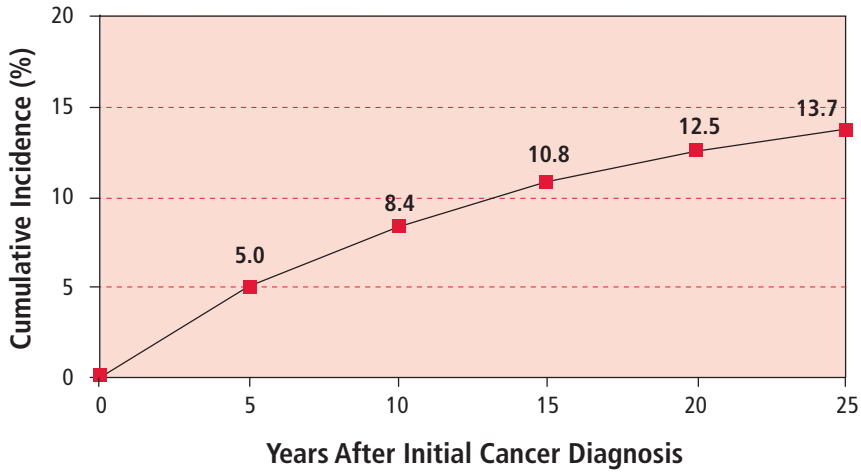


Figure 1. Cumulative incidence of second cancers.

Therapy for an initial cancer among older adults was not associated with a major increase in subsequent cancer risk, although some excesses were identified in specific instances. For example, increased risks were seen for cancers of the lung and esophagus and for sarcomas following initial radiotherapy for breast cancer, whereas elevated risks were noted for acute leukemia after pelvic irradiation for cancers of the cervix and uterine corpus.

Some patterns of multiple cancers reported in the monograph appeared to reflect manifestations of familial cancer syndromes. For example, patients with early-onset colon cancer developed increased risks of cancers of the uterine corpus, ovary, bile ducts, small intestine, and renal pelvis, resembling the features of hereditary nonpolyposis colon cancer (Lynch syndrome) due to inherited mismatch repair genes. The association of breast cancer, sarcomas, and other cancers in children and young adults suggested manifestations of Li-Fraumeni syndrome due to germline mutations of the tumor suppressor gene p53. In addition, the excess of contralateral breast and ovarian cancers among young women with breast cancer were consistent with germline mutations of *BRCA1/2*. Dr. Fraumeni pointed out that "the patterns of multiple primary cancers complement what is seen in familial cancer syndromes and suggest that multiple forms of cancer may have common genetic pathways."

The results from the monograph show clearly that the burden of second cancer occurrence is not borne equally among all cancer survivors. "We hope the monograph will help clinicians in identifying those patients who have an increased risk of developing second cancers," Dr. Tucker said. The patterns of excess risk will inform strategies for early detection and prevention of second cancers, including changes in high-risk lifestyles, such as cigarette smoking, excessive alcohol use, physical inactivity, obesity, and poor diet. The long-term monitoring of cancer survivors will also enable the detection of therapy-related cancers that would assist in making risk-benefit evaluations of specific treatments. Furthermore, the multiple-cancer patterns identified in the monograph should provide leads for further research into the genetic and environmental determinants of cancer. ■

TWENTY YEARS OF COLLABORATIVE BENZENE RESEARCH WITH CHINA

In December, investigators from DCEG and the Chinese Center for Disease Control and Prevention (CDC) celebrated the 20th anniversary of collaboration on studies of occupational exposure to benzene. This binational, multidisciplinary effort was established in 1986 to expand an existing cohort study of occupational benzene exposures led by Dr. Songnian Yin, Dr. Guilan Li, and colleagues from the Institute of Occupational Health and Poison Control (IOHPC) at the Chinese CDC. The expanded study included follow-up of approximately 75,000 Chinese benzene-exposed workers and 35,000 unexposed workers from more than 700 factories and 12 cities. Since that time, "this long-standing collaboration has resulted in a series of high-impact scientific findings that have contributed substantially to our understanding of dose-response relationships and underlying biologic mechanisms of benzene carcinogenicity in humans," said **Martha S. Linet, M.D., M.P.H.,** Chief of the Radiation Epidemiology Branch (REB). Dr. Linet has been working with other DCEG investigators, including **Richard B. Hayes, D.D.S., Ph.D.** (Occupational and Environmental Epidemiology Branch [OEEB]), **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (OEEB), **Mustafa Dosemeci, Ph.D.** (OEEB), **Qing Lan, M.D., Ph.D., M.P.H.** (OEEB), **Roel Vermeulen, Ph.D.** (formerly of OEEB), **Stephen Chanock, M.D.** (Director of the Core Genotyping Facility), **Bu-Tian Ji, M.D., Dr.P.H.** (OEEB), **Graça Dores, M.D.** (formerly of REB), and **Sholom Wacholder, Ph.D.** (Biostatistics Branch).

Many researchers who have worked on the benzene project assembled at the December event.

Dignitaries from the Chinese CDC, Chunming Chen (left front), Guilan Li (left back), Songnian Yin (center back), and Anshou Zhou (right back) with Joseph Fraumeni.

In 1997, a landmark paper was published in the *Journal of the National Cancer Institute.* Lead author Dr. Hayes explained, "We found conclusive evidence that workers exposed to benzene were at significantly higher risk of developing acute nonlymphocytic leukemia (ANLL), myelodysplastic syndromes, and possibly non-Hodgkin lymphoma (NHL)." At doses initially determined to be safe, risk was increased, and for various hematologic outcomes, risk varied by temporal patterns of exposure. "For example, recent exposure in workers was most strongly linked to ANLL and myelodysplastic syndromes," Dr. Hayes added. In parallel research efforts, NCI investigators and their collaborators have made steady progress in elucidating the mechanisms of benzene-induced carcinogenesis and biomarkers of benzene's early effects and in identifying genetic markers of susceptibility. In 2004, a key paper was published in *Science* by Dr. Lan and colleagues showing evidence of hematotoxicity in workers exposed to less than one part per million benzene, the current U.S. occupational standard. To date, findings from both the cohort and molecular epidemiological studies have contributed to lowering the occupational benzene exposure standard in China and have greatly

affected the risk assessment process for environmental benzene exposures in the United States. A new U.S. Environmental Protection Agency (EPA) rule that lowers the concentration of benzene in gasoline was based substantially on this work by DCEG investigators.

The Chinese and U.S. collaborators, as well as dignitaries from the IOHPC and the Chinese CDC, attended an awards ceremony recognizing the key players in this long-standing collaboration. In particular, **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, honored Drs. Yin and Li for their long-term commitment to benzene research in China and for their early case-control study, which served as the inspiration for this 20-year partnership. Other distinguished guests included Dr. Chunming Chen, former director of the Chinese Academy of Preventive Medicine (now known as the Chinese CDC); Dr. Anshou Zhou, vice director of IOHPC; Dr. William Blot, the former lead investigator at NCI, now with the International Epidemiology Institute and Vanderbilt University; Dr. Martyn Smith, University of California, Berkeley; Dr. Robert Rinsky, U.S. Department of Health and Human Services; and Dr. Babasaheb Sonawane, EPA.

Current research activities include an analysis of benzene exposure and risk for selected malignancies in the cohort as part of extended follow-up, further exploration of sources of genetic susceptibility, and related molecular epidemiology studies. This highly successful 20-year international collaboration is poised to provide new insights into the health risks associated with this ubiquitous carcinogen and its mechanisms of action. ■

—Richard B. Hayes, D.D.S., Ph.D.,
Annelie Landgren,
Martha S. Linet, M.D., M.P.H., and
Nathaniel Rothman, M.D., M.P.H., M.H.S.

PARRY RETIRES, NEW INSTITUTIONAL REVIEW BOARD CHAIR APPOINTED

Present and Past IRB Chairs: Maureen Hatch and Dilys Parry.

In January, **Dilys Parry, Ph.D.,** a staff clinician and researcher in the Genetic Epidemiology Branch, retired from NCI after 30 years of service. Dr. Parry served as chair of the NCI Special Studies Institutional Review Board (SSIRB). Her research focused on genetic mapping and clinical studies of neurofibromatosis 2 (NF2); genetic studies of chordoma, a rare bone tumor derived from the notochord; and adult brain tumors. She was a founder of the NIH Interinstitute Medical Genetics Training Program, serving as Associate Director from 1980 to 1994 and Director from 1994 to 1995. She received the NIH Director's Award in 1989 for her role in establishing and maintaining the program. Dr. Parry was a corecipient of the Division's first Mentoring Award in 1989, and she received an NIH Award of Merit in 2002 for developing and directing the Division's interdisciplinary cancer genetics fellowship program. Dr. Parry was appointed to the SSIRB in 1994 and served as vice chair from 2003 to 2006 and as chair from September 2006 until her retirement.

Maureen Hatch, Ph.D., Head of the Chornobyl Research Unit of the Radiation Epidemiology Branch, has been appointed to replace Dr. Parry as chair of the SSIRB. Dr. Hatch joined the SSIRB in 2006 and served as vice chair. Previously, she served on the IRB at Mount Sinai School of Medicine in New York City.

IRBs oversee research conducted on human subjects or specimens from human subjects. The SSIRB is in charge of studies conducted outside the NIH Warren Grant Magnuson Clinical Center. The portfolio of the SSIRB comprises almost 200 protocols involving NCI investigators in a variety of special areas. Many of the protocols involve international collaborations. Notable examples include the HPV vaccine trial being conducted in Costa Rica and case-control studies of esophageal and gastric cancers in China and Iran. Currently, the SSIRB has 12 members drawn from DCEG, Division of Cancer Prevention, Division of Cancer Control and Population Sciences, Epidemiology and Genetics Research Program, and other institutions such as Howard University, who represent a broad array of scientific expertise. In addition, the SSIRB includes one non-scientist who helps ensure that the research appropriately serves the subjects. The SSIRB meets once a month, with assistance from Ms. Lynn Sayers, protocol coordinator, and Ms. Catherine Fox, executive secretary.

"The outstanding members and staff of the Board are certainly one of the reasons I was interested in serving," Dr. Hatch said. "Although I have been with the NCI SSIRB a relatively short time, I have long had an interest in ethical principles of research and have enjoyed the work and responsibilities of IRBs. Serving on the Board provides a valuable view of NCI's research portfolio in the area of 'special studies,' and the new era of 'omics' presents ever new challenges."

LEE MOORE, WORLD TRAVELER, MOLECULAR EPIDEMIOLOGIST

Do you ever wonder where those young "world traveler" types go after they turn in their Eurail passes, hang up their backpacks, and get real jobs?

At least one of them works in DCEG.

Lee E. Moore, Ph.D., caught the travel bug early. Before college, the Milwaukee native spent a summer at the Sorbonne and then a year at France's Université d'Aix-en-Provence. While there, she traveled with a Salvadoran friend and his parents, picking up Spanish skills as she polished her French.

Dr. Moore, who has been a tenure-track investigator in the Occupational and Environmental Epidemiology Branch (OEEB) since 2001, earned a bachelor's degree in molecular biology and French from the University of Wisconsin–Madison before heading overseas again.

Traveling in Indonesia, Dr. Moore met a Frenchman who would later become her husband. (The family—which also includes two sons, aged 10 and 12—now lives in Chevy Chase.) They

Lee Moore

traveled together for two years before landing in San Francisco "because we'd both wanted to go there for a long time," she said.

Dr. Moore's interest in occupational health began at the University of California, Berkeley, where she earned a master's in industrial hygiene and a Ph.D. in environmental health. There, Dr. Moore became involved in arsenic exposure studies in California, Nevada, Chile, Argentina, and India. (Arsenic, a known carcinogen, is naturally found in drinking water.)

Dr. Moore was recruited by **Nathaniel Rothman, M.D., M.P.H., M.H.S.,** a senior investigator in OEEB, while she was working at the University of California, San Francisco, at Berkeley, and at Lawrence Livermore National Laboratory. Upon visiting DCEG, she found that "there were so many projects that I could fit into perfectly—it was amazing!"

Plus, Dr. Moore said, "NCI was the only place where no one looked at my master's degree in industrial hygiene and said, 'What did you do that for?' **Aaron Blair, Ph.D., M.P.H.,** former Chief of OEEB, told me they were happy about the focus of my master's degree—I told him he was the first person to ever say that!"

Working with **Wong-Ho Chow, Ph.D.,** another senior investigator in OEEB, Dr. Moore is analyzing data from the Central and Eastern European kidney cancer study.

"The occupational exposures make this study unique," she explained. "We've looked at trichloroethylene and lead and several genetic pathways that may increase susceptibility to the disease, including genes involved in metabolizing toxic substances, folate metabolism, and vascularization. In tumor tissue, we are analyzing the von Hippel-Lindau gene to determine if risk factors vary by patterns of inactivation. We used comparative genomic hybridization arrays, and we're planning to use expression arrays. We're also planning a study of factors related to survival."

Dr. Moore will also use proteomics to identify biomarkers related to ovarian cancer based on specimens and data from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

DALSU BARIS HONORED BY INTERNATIONAL MYELOMA FOUNDATION

Dalsu Baris speaking at the gala.

Dalsu Baris, M.D., Ph.D., a staff scientist in the Occupational and Environmental Epidemiology Branch, was honored as a member of the international team of scientists who developed the Bank on a Cure® project of the International Myeloma Foundation. The award was presented at the foundation's anniversary gala at the Regent Beverly Wilshire Hotel in Los Angeles on October 21. The International Myeloma Foundation is a nonprofit organization that conducts research and provides education, advocacy, and support for myeloma patients, families, researchers, and physicians. The foundation's Bank on a Cure® project collects and catalogs DNA samples from multiple myeloma patients and their families, which are then analyzed for genetic variations that could contribute to a predisposition to the disease or might influence response to specific treatments.

"It is important to be aware of and minimize potential confounders and biases in study design and data analysis when using proteomics," Dr. Moore said. "It's tricky because there are so many outcomes that there can be false-positive findings."

She notes that in this high-throughput age, consortia are necessary. "People doing this type of research won't be able to do it alone … researchers need to combine studies and work together."

Arsenic exposure is also a major focus of research for Dr. Moore. For this exposure, animal studies are impossible; rodents metabolize arsenic quickly and store the metabolites in their fur. "We must study arsenic exposures in humans," she said.

With data from the New England bladder cancer study, Dr. Moore and colleagues are using biomarkers to compare tumors among persons with and without arsenic or tobacco exposure.

"The tumors have different expression profiles depending on their exposures, but no one really knows what that means yet. For example, tumors with arsenic exposures have big alterations, like a genetic instability syndrome, and all the p53 mutations were in tobacco-exposed tumors."

The group is also studying methylation status as a biomarker in the study. Dr. Moore reported, "We're evaluating methylation status by age, sex, diet, and smoking." So far, the researchers have been unable to confirm previous claims that methylation rates are higher in women, that methylation decreases with age, and that certain genes modify methylation.

"We see less global methylation in bladder cancer cases than in controls," she said. "We can't explain it yet. But it appears to be meaningful."

Dr. Moore has another study she wants to undertake. "With **Kenneth P. Cantor, Ph.D.** (OEEB), I want to look at the cancer risk of people exposed to arsenic *in utero*. Recent studies show these people have very high lung cancer risks, regardless of smoking."

Then the trilingual traveler sighed, still managing to sound optimistic and cheerful. "Sometimes things are not as clear in humans as you would like them to be," she noted. "We're too variable." ■

—Nancy Volkers

LINDSAY MORTON WINS YOUNG SCIENTIST AWARD


Lindsay Morton

Lindsay M. Morton, Ph.D., a research fellow in the Hormonal and Reproductive Epidemiology Branch, was recently selected for the 2006 Young Scientist Award by the Lymphoma Foundation of America (LFA). The award recognizes the accomplishments of a young investigator in the early stages of his or her career whose work is dedicated to examining the causes of lymphoma. Dr. Morton began her work in lymphoma during her graduate studies at Yale University by leading a series of analyses within the population-based Connecticut women's case-control study of non-Hodgkin lymphoma (NHL), looking at how various lifestyle and environmental factors affect the risk of developing this malignancy. Her research supported the role of hepatitis C infection and cigarette smoking in increased incidence of NHL and showed that alcohol was associated with a decreased risk.

Since joining DCEG in 2004 as a postdoctoral fellow, Dr. Morton has played a significant role in designing and conducting analyses within the InterLymph Consortium. As one of the first investigators to use this resource for a pooled analysis, she designed a system to uniformly code questionnaire data and classify tumor types among nine disparate studies, providing the largest combined dataset ever developed for NHL, with approximately 6,500 cases and 9,000 controls. Thus, Dr. Morton reported the most definitive data to date on the increased risk of follicular lymphoma associated with smoking and the decreased risk of B-cell NHL with alcohol use, illustrating that risks do vary among lymphoma subtypes and warrant further investigation regarding the mechanisms responsible. Dr. Morton also initiated the first-ever descriptive analysis of U.S. NHL incidence rates using the updated World Health Organization lymphoma classification system. Her report, which was published in 2005, is considered a foundation paper that is widely cited by NHL researchers.

While Dr. Morton continues her work identifying and analyzing suspected NHL risk factors and determining patterns of risk among lymphoma subtypes in large epidemiologic studies, she has also expanded her work to include molecular studies on newly discovered molecular markers, genetic susceptibility, and gene expression profiling for lymphoma subtypes.

Founded in 1986, LFA is a national organization devoted to helping lymphoma patients and their families. To learn more about the Lymphoma Foundation, visit their web site at www.lymphomahelp.org.

—Alyssa Minutillo, M.P.H.

NCI DIRECTOR'S AWARD WINNERS

Several DCEG staff members won individual and group awards at the annual NCI Director's Awards Ceremony held in October. Dr. John E. Niederhuber, Director of NCI, presented the following NCI Merit Awards:

- **Marianne K. Henderson, M.S.,** Office of Division Operations and Analysis, and **Jim Vaught, Ph.D.,** Office of the Director (OD), along with others across the Institute for their leadership and innovative approaches to address scientific, technical, and policy barriers associated with cancer biorepositories and biospecimens and for developing best practices–based guidelines.
- **Robert N. Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, **Demetrius Albanes, M.D.,** Nutritional Epidemiology Branch and Chief of the Office of Education, **Stephen Chanock, M.D.,** Director of the Core Genotyping Facility (CGF), **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, **Richard B. Hayes, D.D.S., Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB), **Gilles Thomas, M.D., Ph.D.** (CGF), and **Sholom Wacholder, Ph.D.,** Biostatistics Branch (BB), along with Dr. Robert Croyle, Dr. Sandra Melnick, Dr. Edward Trapido, and Dr. Mukesh Verma from the Division of Cancer Control and Population Sciences, for their exceptional leadership in developing the Cohort Consortium—a unique intramural-extramural partnership for conducting research into the genetic and molecular epidemiology of cancer.
- **Katherine A. McGlynn, Ph.D.,** Hormonal and Reproductive Epidemiology Branch (HREB), for her completion of the Servicemen's Testicular Tumor Environmental and Endocrine Determinants (STEED) Study, a novel investigation that should provide etiologic insights regarding this poorly understood tumor.
- **Samantha Nhan** (OD) for her exceptional leadership as Managing Editor of the award-winning DCEG newsletter, *Linkage*.
- **Sophia S. Wang, Ph.D.** (HREB), for her completion of the Study to Understand Cervical Cancer Early Endpoints and Determinants (SUCCEED), aimed at discovering novel biomarkers for cervical carcinogenesis among HPV-infected women.

Merit Award Winners: Top photo, John Niederhuber, Joseph Fraumeni, Demetrius Albanes, Stephen Chanock, Richard Hayes, Sholom Wacholder, Edward Trapido, Sandra Melnick, Robert Hoover, Robert Croyle, and Mukesh Verma. Left bottom, Samantha Nhan with John Niederhuber. Right bottom, Sophia Wang with John Niederhuber.

In addition, **Eric A. Engels, M.D., M.P.H.,** Viral Epidemiology Branch, received the NCI Mentor of Merit Award for his contribution to a critical element of DCEG's mission—training the next generation of scientists. Each year, the winner of this award is chosen from among those nominated by NCI postdoctoral fellows.

Nathaniel Rothman, M.D., M.P.H., M.H.S. (OEEB), received the Outstanding Service Medal for his service to the U.S. Public Health Service Commissioned Corps.

Finally, several staff members were recognized for their dedication to the federal government and received Year-in-Service Awards. **Susan S. Devesa, Ph.D.** (BB), reached 40 years of service, **B.J. Stone, Ph.D.** (BB), 30 years, and **Mark H. Greene, M.D.,** Clinical Genetics Branch, 20 years. The following staff members have served 10 years: **Ethel S. Gilbert, Ph.D.,** Radiation Epidemiology Branch, **Maria Teresa Landi, M.D., Ph.D.,** Genetic Epidemiology Branch (GEB), **Mary Lou McMaster, M.D.** (GEB), and Ms. Nhan. ■

NEW DCEG WOMEN SCIENTIST ADVISORS ELECTED

Montserrat García-Closas, M.D., Dr.P.H., of the Hormonal and Reproductive Epidemiology Branch (HREB), has been elected DCEG's new Women Scientist Advisor (WSA), and **Ann Hsing, Ph.D.** (HREB), the new WSA-Alternate. **Lynn R. Goldin, Ph.D.,** of the Genetic Epidemiology Branch, and **Debra Silverman, Sc.D.,** of the Occupational and Environmental Epidemiology Branch, have ended their terms as DCEG's WSA and WSA-Alternate.

As WSAs, Drs. Goldin and Silverman held a DCEG-wide forum, "Navigating the system," focusing on career advancement in DCEG. Other events included brown bag lunches for each branch and separate group meetings for fellows and for tenure-track, tenured, and staff scientists to identify the concerns of women scientists. The WSA or her alternate participates in DCEG's Senior Advisory Group and search committees and organizes meetings at the NCI Intramural Scientific retreats. In addition to their activities within the Division and the Institute, the WSAs also participate in the NIH-wide Women Scientists Committee.

Over the past two years, the DCEG WSAs have organized meetings with distinguished scientists visiting the Division, including Dr. Nancy Mueller (Harvard School of Public Health), Dr. Valerie Beral (University of Oxford), Dr. Olofunmilayo Olopade (University of Chicago Pritzker School of Medicine), Dr. Eve Roman (University of York), and Dr. Elizabeth Holly (University of California, San Francisco). These meetings have been informative and entertaining, with the scientists sharing insights on their work lives and successful career trajectories.

Present and Past WSA Representatives and Alternates: Ann Hsing, Montserrat García-Closas, Lynn Goldin, and Debra Silverman.

Promotion Type	Average Time to Promotion (Years)	
	Women	Men
Fellow to Tenure-track	4.6	5.1
Tenure-track to Tenured	4.1	4.0
GS-14 to GS-15	4.4	5.0

Over the past two years, the DCEG WSAs have organized meetings with distinguished scientists visiting the Division … These meetings have been informative and entertaining, with the scientists sharing insights on their work lives and successful career trajectories.

The WSAs meet annually with **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, and **Shelia Hoar Zahm, Sc.D.,** DCEG Deputy Director, to review the concerns of women scientists and formulate plans on how to address them. They discuss mentoring, salaries, promotions, and communication across the Division and suggest improvements in these areas. Annually, DCEG also analyzes principal investigator salaries by sex and year since degree, separately for investigators with medical degrees and those with academic doctorates, and examines the data for any signs of bias. Recently, Dr. Zahm also developed "time-to-promotion" data for DCEG from 1995 to 2006 by sex, and the results indicated no evidence of disparities. ■

—Lynn R. Goldin, Ph.D.

NEW LECTURE SERIES LAUNCHED ON PUBLIC HEALTH GENOMICS

Evidence suggests that the genetic contribution to most chronic diseases is likely to derive from multiple genes, each with a small-to-moderate effect, strongly influenced by individual behaviors and other environmental factors.

Genomics—the study of the genome, its sequence, and its expression—can analyze which genes are expressed in a given disease and/or environmental state and, when linked to a population-wide research program, can sort out the complicated underlying genetic contributions. Translating such a vast amount of information into public health practice, however, presents great challenges. What meaningful advice could be provided to the public about genetic risks? How could the information be used to improve the public health? How could such legitimate scientific information be used to counter so-called "nutrigenetic" tests that purport to characterize the consumer's genetic profile and offer individualized nutritional and vitamin supplement advice and products?

With these and other questions in mind, an interdisciplinary seminar series titled Public Health Genomics: Closing the Gap between Human Genome Discoveries and Population Health has been launched. Organized by Dr. Muin J. Khoury, Director of the National Office of Public Health Genomics at CDC and sponsored by DCEG and the Division of Cancer Control and Population Sciences (DCCPS), the monthly seminars explore various topics at the intersection of genomics, medicine, and public health, with an emphasis on translating genomic discoveries into effective clinical and public health interventions. CDC, the National Human Genome Research Institute (NHGRI), the National Institute of Child Health and Human Development, and the NIH Office of Behavioral and Social Sciences Research (OBSSR) are cosponsors of the series.

"The overarching vision for public health genomics is the effective and responsible translation of genome-based knowledge and technology for the benefit of population health," Dr. Khoury stated. "For this to occur, there needs to be a real partnership between basic sciences, clinical medicine, and public health throughout the translational research continuum. Using a population health perspective, this yearlong series explores in some detail the interaction among various scientific disciplines that are ultimately needed to reap the benefits of exciting scientific discoveries."

"This series … informs the process of gene discovery and its translation to clinical practice and public health measures."

The series builds on existing NCI-CDC research collaborations in several areas. These include the NHANES III investigation of genetic variants and their clinical and biochemical phenotypic correlates and the Human Genome Epidemiology Network, established to accelerate the knowledge-based development of genetic variation and common diseases using cancer as a prototype. The seminars will also draw on the NCI cohort, case-control, and family-based consortia that develop and update "field synopses" for cancer risk in relation to genetic variation and apply family history data and other tools for the prediction and prevention of various cancers.

"The integration of new genomic technologies into epidemiologic designs is greatly accelerating our understanding of the genetic underpinnings of cancer induction and progression," said **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG. "This series summarizes the state of our knowledge at this time and also informs the process of gene discovery and its translation to clinical practice and public health measures."

The lectures draw upon expertise and leadership in the fields of public health, population genetics and genomics, cancer epidemiology, and gene-based prevention strategies. Speakers include Dr. Khoury; DCEG scientists **Stephen Chanock, M.D.** (Director of the Core Genotyping Facility), **Robert N. Hoover, M.D., Sc.D.** (Director of the Epidemiology and Biostatistics Program), and **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (Occupational and Environmental Epidemiology Branch); and Dr. David Abrams (OBSSR), Dr. Linda Bradley (CDC), Dr. Alan Guttmacher (NHGRI), Dr. Kathy Hudson (Johns Hopkins University), Dr. Jon Kerner (DCCPS), Dr. Teri Manolio (NHGRI), Dr. Colleen McBride (NHGRI), Dr. Charles Rotimi (Howard University), Dr. Louise Wideroff (DCCPS), and Dr. Paula Yoon (CDC).

The series includes nine presentations, the last one in November 2007. Interested researchers and public health officials can learn more about these lectures, including an updated list of topics and speakers, videocast information, and other details at http://dceg.cancer.gov/GenomicsCourse. ■

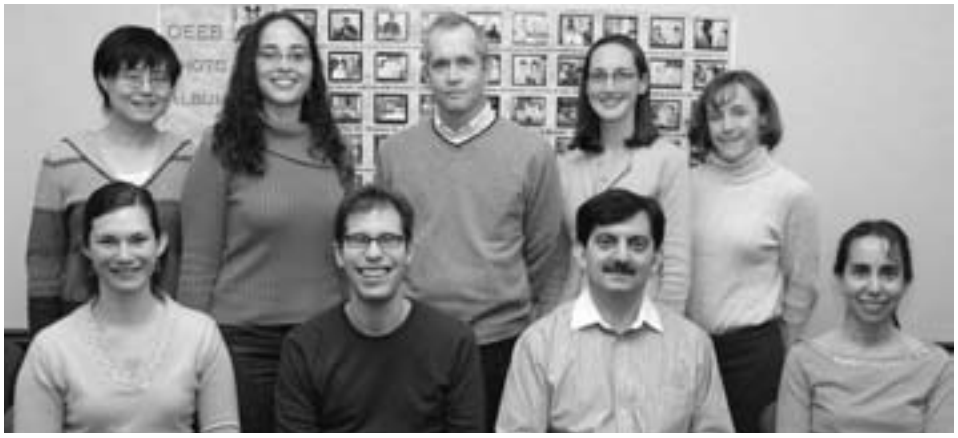
—Demetrius Albanes, M.D., and Deborah Winn, Ph.D.

ANNUAL NCI INTRAMURAL SCIENTIFIC RETREAT HELD

The 11th Annual NCI Intramural Scientific Retreat was held January 9 at the Bethesda North Marriott Hotel and Conference Center. More than 600 participants, including several members of the NCI Executive Committee and advisory boards, attended. The retreat included two poster sessions and three award lectures and provided a forum for sharing research and fostering collaborations between intramural investigators across NCI, core facilities and research support services, and NCI's scientific advisory boards.

John Niederhuber, Alice Whittemore, and Joseph Fraumeni.

John Niederhuber and Joseph Fraumeni.



DCEG Innovation Award Winners: (front) Mia Gaudet, Neal Freedman, Farin Kamangar, Rachael Stolzenberg-Solomon; (back) Rose Yang, Jonine Figueroa, William Anderson, Lindsay Morton, and Sonja Berndt.

Dr. Alice Whittemore, professor at Stanford University School of Medicine and 6th Annual Rosalind E. Franklin awardee for excellence in cancer research by women scientists, lectured on "Preventing deaths from breast and ovarian cancer."

Dr. Frederick W. Alt, Charles A. Janeway Professor of Pediatrics at Harvard Medical School, received the 11th Annual Alfred G. Knudson Award in cancer genetics. His award lecture was titled "Synapsis and joining pathways that mediate class switch recombination and suppress translocations."

DCEG Director **Joseph F. Fraumeni, Jr., M.D.,** received the 3rd Annual Alan S. Rabson Award for excellence in intramural research. Dr. Fraumeni's lecture on "Genes and the environment in cancer causation" summarized what has been learned in cancer epidemiology over the past 40 years and highlighted many contributions by the Division's researchers. The talk discussed the excitement of being in such a promising time in epidemiology, when the power of genomics and molecular approaches can be incorporated into carefully thought-out strategies.

The NCI Women Scientist Advisors (WSAs) held a luncheon meeting, during which Dr. Joan Schwartz, NIH Office of Intramural Research, unveiled the results of the NIH Task Force Report on the current status of intramural women scientists. The NCI WSAs, including DCEG representatives **Lynn R. Goldin, Ph.D.,** a senior investigator in the Genetic Epidemiology Branch (GEB), and **Debra Silverman, Sc.D.,** a senior investigator in the Occupational and Environmental Epidemiology Branch (OEEB), hosted a question-and-answer session following the presentation.

Finally, NCI Director Dr. John E. Niederhuber presented the 2007 NCI Director's Intramural Innovation Awards. Designed to support the development of highly innovative approaches and technologies aimed at significant cancer-related problems, the program offers one-time awards for use in the 2007 fiscal year at two levels: Principal Investigator (PI) Awards for tenure-track or recently tenured investigators (within five years of tenure) and Career Development Awards to postdoctoral fellows, staff scientists, staff clinicians, and senior scientists. **Rose Yang, Ph.D., M.P.H.** (GEB), **William F. Anderson, M.D., M.P.H.,** Biostatistics Branch, and **Rachael Stolzenberg-Solomon, M.P.H., Ph.D.,** Nutritional Epidemiology Branch (NEB), were DCEG recipients of PI Awards; **Neal Freedman, Ph.D., M.P.H.** (NEB), **Lindsay M. Morton, Ph.D.,** Hormonal and Reproductive Epidemiology Branch (HREB), **Sonja Berndt, Pharm.D., Ph.D.** (OEEB), **Mia Gaudet, Ph.D.** (HREB), **Farin Kamangar, M.D., M.P.H.** (NEB), and **Jonine Figueroa, Ph.D., M.P.H.** (HREB), received Career Development Awards. ■

—Elyse Wiszneauckas and Marianne K. Henderson, M.S.

DCEG TENURE-TRACK INVESTIGATOR RETREAT HELD

DCEG held its third tenure-track investigator retreat in October at the Natcher Conference Center. Organized by Committee of Scientists' representatives **Eric A. Engels, M.D., M.P.H.,** Viral Epidemiology Branch, and **Mary H. Ward, Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB), the full-day retreat provided information about the tenure process in the intramural research program and offered suggestions on how to optimize time on the tenure track. Approximately 20 tenure-track investigators, their mentors, and senior scientists from DCEG participated in the event. **Joseph F. Fraumeni, Jr., M.D.,** Division Director, opened the retreat with lessons on "The Road to Tenure." Dr. Fraumeni described specific measures of progress that are important for achieving tenure at NIH. Emphasis was placed on the philosophy of research in DCEG and the unique characteristics of the intramural research program that create a setting for high-impact, high-quality, and distinctive science. Dr. Barry Kramer, Associate NIH Director for Disease Prevention, shared his insights on how to craft a successful tenure package based on his experience with the NIH Central Tenure Committee as cochair with Dr. Fraumeni of the NIH Epidemiology and Biometry Review Panel. Dr. Kramer's presentation was followed by a panel discussion with Dr. Fraumeni, **Margaret Tucker, M.D.,** Director of the Human Genetics Program and Chief of the Genetic Epidemiology Branch (GEB), and **Ann Hsing, Ph.D.,** a senior investigator in the Hormonal and Reproductive Epidemiology Branch.

The discussion was followed by a panel on mentoring comprising **Neil Caporaso, M.D.** (GEB), **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program, and **Debra Silverman, Sc.D.** (OEEB). Dr. Hartge asked each tenure-track investigator to estimate the quantity and quality of mentoring they provide and receive. The results revealed that tenure-track investigators think they provide less mentoring than they receive, but as Dr. Hartge stated, "It appears that you falsely underrated yourselves. You all put many more hours into mentoring and provide it at a higher quality than you give yourselves credit for." Members of the panel emphasized that mentoring involves both discussions about science and helping with decisions about the right career path. One panelist said that mentoring should mostly be about asking the important and difficult questions.

The retreat concluded with a talk by Dr. Margaret Spitz, chair of the Department of Epidemiology at the University of Texas M.D. Anderson Cancer Center, titled "Epidemiology and your future: Adjusting for career confounders." Dr. Spitz expounded on the concept of "integrative epidemiology," which emphasizes that the predisposition to cancer is one end of a spectrum that culminates in tumor behavior and response to therapy. Providing several examples from her own research on lung cancer, she pointed to the need for interdisciplinary collaborations and the resulting challenges of demonstrating scientific independence and individual contribution to collaborative research projects. Dr. Spitz reviewed the "Ten commandments for academic success and getting tenure" (see box). In a light-hearted but informative way, she illustrated each of them by describing an instance in her own career when she failed to follow the commandment. Dr. Spitz concluded her talk by stating, "This is an exciting time to be a cancer epidemiologist. You are in the right place at the right time. Go for it!" ■

—Eric A. Engels, M.D., and Mary H. Ward, Ph.D.

Tenure-track investigator retreat participants with Margaret Spitz (second from right) and Joseph Fraumeni (right).

Ten Commandments for Academic Success and Getting Tenure

- Honor thy priorities.
- Thou shalt recognize opportunity when it knocks.
- Thou shalt be confident and have focus.
- Thou shalt take feedback with grace.
- Thou shalt learn to network.
- Honor thy good mentors.
- Thou shalt act with integrity and collegiality.
- Thou shalt learn when to say "no."
- Thou shalt have fun.
- Thou shalt not listen to other people's tips but follow thine own instincts.

MELDING CANCER EPIDEMIOLOGY AND GENOMICS

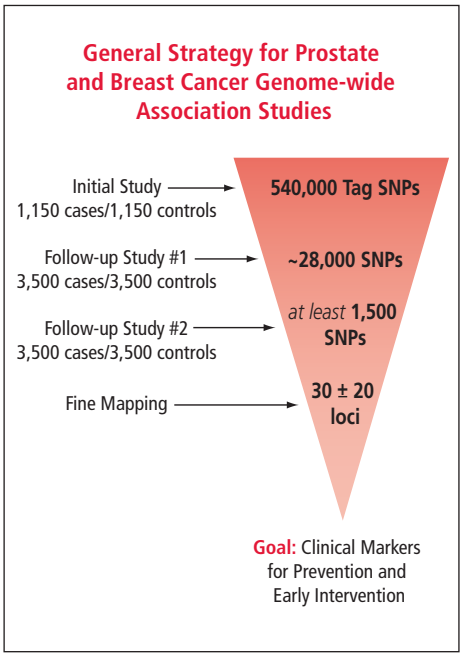
At the December meeting of the National Cancer Advisory Board (NCAB), DCEG scientists presented the progress being made to harness the power of new genomic technology through epidemiologic studies designed to uncover common gene variants or single nucleotide polymorphisms (SNPs) that contribute to cancer susceptibility.

Together with colleagues in the of Cancer Control and Population Sciences and the Office of Cancer Genomics, DCEG has joined forces with extramural collaborators to form strategic partnerships that link epidemiologists; genomicists; and other investigators from the clinical, basic, and population sciences to uncover gene-environment interactions that could be responsible for a large proportion of cancer cases. In remarks to the NCAB, **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, explained, "This transdisciplinary team-based approach responds to a growing consensus in the scientific community that realizing the full potential of genomic and other new technologies requires their integration into robust, large-scale epidemiologic studies."

This can be accomplished through consortia that combine resources of several large cohort and/or case-control studies in a coordinated approach that allows rapid replication of positive findings. One such unique partnership is the Cohort Consortium—an international collaboration of investigators responsible for 23 population cohorts that include 1.2 million individuals. **Robert N. Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, who spearheaded development of this consortium, demonstrated how it provides an integrated framework for nested case-control studies of specific cancers and allows for the systematic evaluation of molecular and biochemical biomarkers of susceptibility and disease.

Other speakers described two approaches to identifying cancer susceptibility genes: the pathway-driven approach and genome-wide association studies (GWAS). The first technique involves studies that investigate risks associated with candidate genes selected on the basis of known function or biologic plausibility. As an example of this approach, **Montserrat García-Closas, M.D., Dr.P.H.,** an investigator in the Hormonal and Reproductive Epidemiology Branch, presented results from the Breast Cancer Association Consortium and a case-control study conducted in Spain that showed that SNPs in candidate genes *NAT2* and *GSTM1* were associated with increased risk of bladder cancer and that *NAT2* modified the risk due to cigarette smoking. Although the relative risks were modest, these SNPs are common among bladder cancer patients and could contribute to nearly one-third of the cases. These results were published in *Lancet* in 2006.

In contrast, GWAS use the latest technologies to "interrogate" the entire genome. **Stephen Chanock, M.D.,** Director of the Core Genotyping Facility, described the Cancer Genetic Markers of Susceptibility (CGEMS) project, which uses high-throughput technology to identify and validate susceptibility genes for breast and prostate cancers. The potential associations identified will be validated in future studies to eliminate false positives due to chance. To date, the CGEMS team of DCEG and extramural epidemiologists, statisticians, and genomicists have completed GWAS on 1,200 prostate cancer cases and controls, and posted the data on NCI's caBIG web site (http://cabig.cancer.gov). It is anticipated that the initial results for breast cancer will be posted in early 2007, and plans are under way to launch a similar scan for genes involved in pancreatic cancer.



These highly collaborative strategies will provide the scientific community with unprecedented opportunities to understand cancer susceptibility mechanisms, including gene-environment interactions, and thus inform new ways to accelerate the prevention, early detection, and treatment of cancer. ■

—Catherine McClave, M.S.

MACARTHUR FELLOW OLOPADE VISITS DCEG

In September, Dr. Olofunmilayo (Funmi) Olopade, Walter L. Palmer Distinguished Service Professor of Medicine at the University of Chicago Pritzker School of Medicine, came to DCEG as a Visiting Scholar.

Joseph Fraumeni, Olofunmilayo Olopade, and Mark Greene.

Dr. Olopade is known worldwide for her role in developing the clinical cancer genetics field and defining the genetic underpinnings of breast cancer disparities in the United States. Among her numerous accolades, Dr. Olopade was recognized by the MacArthur Foundation in 2005 with a "Genius Award" for her work in "translating findings on the molecular genetics of breast cancer in African and African American women into innovative clinical practices in the United States and abroad."

Dr. Olopade graduated from the University of Ibadan, Nigeria, in 1980 and began her medical career soon afterward when she came to the United States to complete an internship and residency at Cook County Hospital in Chicago. After a fellowship in hematology and oncology at the University of Chicago, Dr. Olopade completed her postdoctoral research in the laboratory of Dr. Janet Rowley, where she studied cancer susceptibility genes on chromosome 9. Because she combined an understanding of both the clinical and molecular aspects of cancer, she was uniquely qualified to work in the new field of clinical cancer genetics, created when the first breast cancer susceptibility gene, *BRCA1,* was identified in 1994. In addition to her laboratory work, Dr. Olopade was a physician in the University of Chicago Cancer Risk Clinic and saw many patients seeking genetic testing and preventive therapy for breast cancer. Thus began her productive, innovative research program on the genetic causes of breast cancer, in which she has elucidated many of the reasons for disparities in risk and mortality among racial groups. Dr. Olopade has also explored the clinical implications of genetic testing risk assessments and developed preventive interventions among populations with genetic susceptibility.

The visit to DCEG commenced with Dr. Olopade's Visiting Scholar Seminar, titled "Tracking breast cancer susceptibility in the African Diaspora," in which she described her work within families at high risk for breast cancer in the United States and how her findings led her to expand her research into the African population.

"When I began my research on breast cancer in South Side Chicago, giving genetic tests and risk assessments to my female clinic patients, both African American and Caucasian, I was struck by the *BRCA1* and *BRCA2* mutation incidences across ethnic groups," Dr. Olopade recalled. Using pedigree studies, she illustrated familial cancer patterns, especially in early-onset, often fatal breast cancers among black women. Dr. Olopade became "increasingly aware that the survival from early breast cancer in black women was poor relative to white women," and she resolved to explain this difference.

This question led her back to her native Nigeria, where she was determined to identify the reasons for familial patterns. "I believed that patterns of genetic variation were unique to that region of the African population, so we started the Nigeria Breast Cancer Project in 2002, initially as a case-control study of 1,000 hospital-based cases and controls," she explained. Dr. Olopade and her team performed genetic analyses to examine mutations in the *BRCA1/2* genes that convey a high level of risk, analyzing associations between mutations and various environmental factors, and comparing their findings with populations in both the United States and elsewhere in Africa. "Our goals were to characterize the mutation haplotypes that account for the overrepresentation of certain

aggressive breast cancer subtypes in African and African American women. I hope to identify biomarkers within these genes that will lead to new therapies effectively targeting these aggressive tumor types," Dr. Olopade said.

Dr. Olopade also described new projects, including an investigation of gene expression profile differences in breast cancer from African American and white women, which could enable researchers to link certain cancer phenotypes to specific *BRCA1/2* mutations and to determine cancer subtype variations by race. She is also launching new collaborations to explore the psychosocial effects of race and culture on women's health; risk of breast cancer; and the decisions women make about cancer screening, diagnosis, and treatment.

At the conclusion of her seminar, Dr. Olopade was awarded the DCEG Visiting Scholar Award in recognition of her vision and leadership in cancer genetics.

Following the seminar, DCEG fellows and tenure-track investigators met with Dr. Olopade at a brown bag lunch to learn about her career and benefit from her professional wisdom. "I encourage you to seek opportunities to become well known in your field and to explore your interests to find the research area you're passionate about," Dr. Olopade told the group. "It's much easier to go to work when you love what you're doing."

Over the remainder of her visit, Dr. Olopade participated in several forums and discussions, the first of which was led by **Mitchell H. Gail, M.D., Ph.D.,** Chief of the Biostatistics Branch, titled "Research issues related to mammographic density as a breast cancer risk factor."

She later attended a roundtable led by **Mark H. Greene, M.D.,** Chief of the Clinical Genetics Branch (CGB), on "Research issues related to ongoing family studies projects," in which DCEG investigators **Sharon A. Savage, M.D.** (CGB), **Blanche P. Alter, M.D., M.P.H.** (CGB), **Jorge R. Toro, M.D.,** Genetic Epidemiology Branch (GEB), and **Rose Yang, Ph.D., M.P.H.** (GEB), presented highlights of their current projects.

In a session moderated by **Arthur Schatzkin, M.D., Dr.P.H.,** Chief of the Nutritional Epidemiology Branch (NEB), investigators **Philip E. Castle, Ph.D., M.P.H.,** Hormonal and Reproductive Epidemiology Branch (HREB), **Ola Landgren, M.D., Ph.D.** (GEB), **James V. Lacey, Jr., Ph.D.** (HREB), and **Sanford M. Dawsey, M.D.** (NEB), presented selected highlights of nonfamilial DCEG research projects. The DCEG Women Scientists Advisory Committee hosted a brown bag lunch on the second day of Dr. Olopade's visit to discuss the work environment for female scientists in the competitive field of biomedical research. Dr. Olopade shared important bits of advice given to her during her early days as a fellow and encouraged fellows to look to their mentors and other senior staff for practical advice. "Sometimes the most obvious or simple suggestions can make all the difference when it comes to balancing work life and having a family," she told them.

She closed out her visit with a research forum, moderated by **Lynn R. Goldin, Ph.D.** (GEB), titled "Future directions in familial cancer research: Syndrome(s) less well traveled?"

Dr. Olopade's visit to DCEG was preceded by her presentation of the 2006 Margaret Pittman Lecture in the NIH Director's Wednesday Afternoon Lecture Series. This lecture honors Dr. Pittman, the first female laboratory chief, for her outstanding research accomplishments at NIH. ■

— Alyssa Minutillo, M.P.H.

TRANSLOCATION WORKSHOP

In October, **Charles Rabkin, M.D.,** a senior scientist in the Viral Epidemiology Branch, and Dr. Siegfried Janz, a staff scientist in the CCR Laboratory of Genetics, hosted an NCI workshop entitled "Mechanisms and consequences of chromosomal translocation." Thirty-seven international experts participated in this two-day conference, which was partially supported by the NIH Office of Rare Diseases. The first half of the workshop was devoted to recent findings on the molecular mechanisms of these translocations with a particular focus on MYC-IGH, a model system that elucidates translocations involving the immunoglobulin switch region, a hallmark of B-cell malignancies. The second half included pathologic consequences and associations with risks of hematopoietic and other malignancies. To share the proceedings with others interested in this important disease process, the invited papers will be published as a monograph in the *Journal of the National Cancer Institute.*

Translocation workshop participants *(Photograph Credit: Alexander Kovalchuk)*

SCIENTIFIC HIGHLIGHTS

BREAST CANCER

ATM Missense Mutations

A total of 22 *ATM* variants were studied in relation to breast cancer; 18 variants were analyzed in one of two large population-based studies from the United States and Poland, and 4 variants were analyzed in all 2,856 breast cancer cases and 3,344 controls from the two studies. The missense mutation *Ser49Cys (c.146C>G, p.S49C)*, carried by approximately 2% of subjects, was more common in cases than controls in both study populations (combined odds ratio [OR] = 1.69; CI = 1.19–2.40; $p = 0.004$). Another missense mutation occurring at approximately 2% frequency, *Phe858Leu (c.2572T>C, p.F858L)*, was associated with a significantly increased risk in the U.S. study but not in Poland and had a combined OR of 1.44 (CI = 0.98–2.11; $p = 0.06$). Because of the missense mutations' low frequency, even larger sample sizes are required to more firmly establish these associations. **(Stredrick DL, García-Closas M, Pineda MA, Bhatti P, Alexander BH, Doody MM, Lissowska J, Peplonska B, Brinton LA, Chanock SJ, Struewing JP, Sigurdson AJ. The *ATM* missense mutation p.Ser49Cys (c.146C>G) and the risk of breast cancer. *Hum Mutat* 2006;27:538–544)**

Evaluation of Gail Model in Italy

Data from a multicenter case-control study in Italy and from Italian cancer registries were used to develop a model (IT-GM) that uses the same risk factors as the Gail model 2 (GM) for predicting absolute risk of invasive breast cancer. The accuracies of the IT-GM and the GM were evaluated using independent data from the Florence-European Prospective Investigation into Cancer and Nutrition cohort. The overall ratios of expected to observed numbers of incident breast cancers (E/O) were 0.96 (CI = 0.84–1.11) and 0.93 (CI = 0.81–1.08) for the IT-GM and the GM, respectively. The IT-GM was somewhat better calibrated than the GM in women younger than 50 years, but the GM was better calibrated when age at first live birth categories were considered (e.g., 20- to 24-year age-at-first-birth category: E/O = 0.68, CI = 0.53–0.94 for the IT-GM and E/O = 0.75, CI = 0.58–1.03 for the GM). The concordance statistic was approximately 59% for both models, with CIs indicating that the models performed better than pure chance. There was no significant evidence of miscalibration overall for either the IT-GM or the GM, and the models had equivalent discriminatory accuracy. **(Decarli A, Calza S, Masala G, Specchia C, Palli D, Gail MH. Gail model for prediction of absolute risk of invasive breast cancer: Independent evaluation in the Florence-European Prospective Investigation into Cancer and Nutrition cohort. *J Natl Cancer Inst* 2006;98:1686–1693)**

Variation in *COMT*

To comprehensively characterize genetic variation in *catechol-O-methyltransferase* (*COMT*), a total of 11 haplotype-tagging single nucleotide polymorphisms (htSNPs), including *COMT Val^{158}Met*, were selected based on the resequencing and dense genotyping approach of the Breast and Prostate Cancer Cohort Consortium and genotyped in a population-based, case-control study in Poland (1,995 cases and 2,296 controls). SNPs were not significantly associated with risk. Overall differences in the haplotype distribution between cases and controls were assessed using a global score test. The TGAG haplotype (frequent in 4.3% of controls), in a linkage disequilibrium (LD) block that included the 3' untranslated region of *COMT*, was associated with breast cancer risk (OR = 1.29; CI = 1.06–1.58) compared with the most common haplotype, TGAA; however, the global test for haplotype associations was not significant ($p = 0.09$). Haplotypes in another LD block, which included *COMT Val^{158}Met*, were not associated with breast cancer risk (global $p = 0.76$). These data do not support a substantial overall association between *COMT* haplotypes and breast cancer. **(Gaudet MM, Chanock S, Lissowska J, Berndt SI, Peplonska B, Brinton LA, Welch R, Yeager M, Bardin-Mikolajczak A, García-Closas M. Comprehensive assessment of genetic variation of *catechol-O-methyltransferase* and breast cancer risk. *Cancer Res* 2006;66:9781–9785)**

GASTRIC CANCER

Helicobacter pylori

To assess details of the association of *Helicobacter pylori* with gastric cancer, a prospective nested case-control study of *H. pylori* serology was conducted among subjects selected from the 29,133 50- to 69-year-old males recruited into the Alpha-tocopherol, Beta-carotene (ATBC) Cancer Prevention Study. Baseline serum samples from 234 cases (173 with noncardia gastric cancers and 61 with gastric cardia cancers) diagnosed between 1985 and 1999 and 234 age-matched controls were assayed for antibodies against *H. pylori* whole-cell and CagA antigens. *H. pylori* seropositivity was strongly associated with risk of noncardia gastric cancer (OR = 7.9; CI = 3.0–20.9) but was inversely associated with risk of gastric cardia cancer (OR = 0.31; CI = 0.11–0.89). Absolute risks of noncardia gastric and cardia gastric adenocarcinomas in the *H. pylori*–positive participants of this cohort were 63 and 12 per 100,000 person-years, respectively, whereas corresponding rates in *H. pylori*–negative

participants were 8 and 37 per 100,000 person-years. *H. pylori* prevalence during the past century may have contributed to lower rates of noncardia cancer and higher rates of cardia cancer in Western countries. **(Kamangar F, Dawsey SM, Blaser MJ, Perez-Perez GI, Pietinen P, Newschaffer CJ, Abnet CC, Albanes D, Virtamo J, Taylor PR. Opposing risks of gastric cardia and noncardia gastric adenocarcinomas associated with *Helicobacter pylori* seropositivity. *J Natl Cancer Inst* 2006;98:1445–1452)**

HIV-RELATED MALIGNANCIES

Female Cancers in AIDS Patients

Linked HIV/AIDS and cancer surveillance data in 12 U.S. regions were used to compare breast and reproductive cancer risks in people with AIDS to those in the general population. Among women with AIDS, 313 developed breast cancer (standardized incidence ratio [SIR] = 0.69; CI = 0.62–0.77), 42 developed ovarian cancer (SIR = 1.05; CI = 0.75–1.42), and 31 developed uterine corpus cancer (SIR = 0.57; CI = 0.39–0.81). Uterine cancer risk was reduced after age 50 (SIR = 0.33). Breast cancer risk was reduced significantly both before (SIR = 0.71) and after (SIR = 0.66) age 50 and was lower for local and regional (SIR = 0.54) than for distant (SIR = 0.89) disease. Breast cancer risk varied little by CD4 count (p = 0.47) or AIDS-relative time (p = 0.14) or after adjustment for established cancer risk factors. However, it increased significantly between 1980 and 2002 (p = 0.003), approaching the risk of the general population (see Figure 1). The authors concluded that the cancer deficit reflected direct or indirect effects of HIV/AIDS and that anti-HIV therapy reduced these effects. **(Goedert JJ, Schairer C, McNeel TS, Hessol NA, Rabkin CS, Engels EA; HIV/AIDS Cancer Match Study. Risk of breast, ovary, and uterine corpus cancers among 85,268 women with AIDS. *Br J Cancer* 2006;95:642–648)**

HIV/AIDS and Hodgkin Lymphoma

Hodgkin lymphoma (HL) incidence increases in persons with HIV/AIDS (PWHAs), but HL incidence in PWHAs has unexpectedly increased since highly active antiretroviral therapy (HAART) was introduced. Using linked nationwide HIV/AIDS and cancer registry data from 1980 through 2002 and immunity levels assessed by CD4 T-lymphocyte counts at AIDS onset, annual HL incidence rates were calculated for 4 through 27 months after AIDS onset. During 477,368 person-years of follow-up in 317,428 persons with AIDS (PWAs), 173 HL cases occurred (36.2 per 100,000 person-years). Incidence was significantly higher between 1996 and 2002 than earlier. Incidence in PWAs with 150 to 199 CD4 cells/μL was 53.7 per 100,000 person-years, whereas in PWAs with fewer than 50 CD4 cells/μL, it was 20.7 per 100,000 person-years (p = 0.002). For each HL subtype, incidence decreased with declining CD4 counts, but nodular sclerosing HL decreased more precipitously than mixed cellularity HL, thereby increasing the proportion of mixed cellularity HL seen in PWAs. Thus, HL incidence is lower with severe immunosuppression than with moderate immunosuppression, and HAART-related improvements in CD4 counts likely explain the increasing HL incidence in PWAs observed since 1996. With more severe immunosuppression, nodular sclerosing HL becomes infrequent, explaining the higher proportion of mixed cellularity HL found in PWAs. **(Biggar RJ, Jaffe ES, Goedert JJ, Chaturvedi A, Pfeiffer R, Engels EA. Hodgkin lymphoma and immunodeficiency in persons with HIV/AIDS. *Blood* 2006;108:3786–3791)**

Lung Cancer Incidence in HIV-infected Individuals

Data from a retrospective cohort study conducted at an HIV specialty clinic in Baltimore for the time period 1989 to 2003 were used to characterize lung cancer incidence among HIV-infected individuals, examine whether cancer risk was related to HIV-induced immunosuppression, and assess whether the high prevalence of smoking explained elevated risk. Thirty-three lung cancers were observed among 5,238 HIV-infected patients (incidence: 170 per 100,000 person-years). Incidence increased with age ($p < 0.0001$) but did not differ by sex, race, or CD4 count. The SIR was 4.7 (CI = 3.2–6.5) vs. an urban reference population

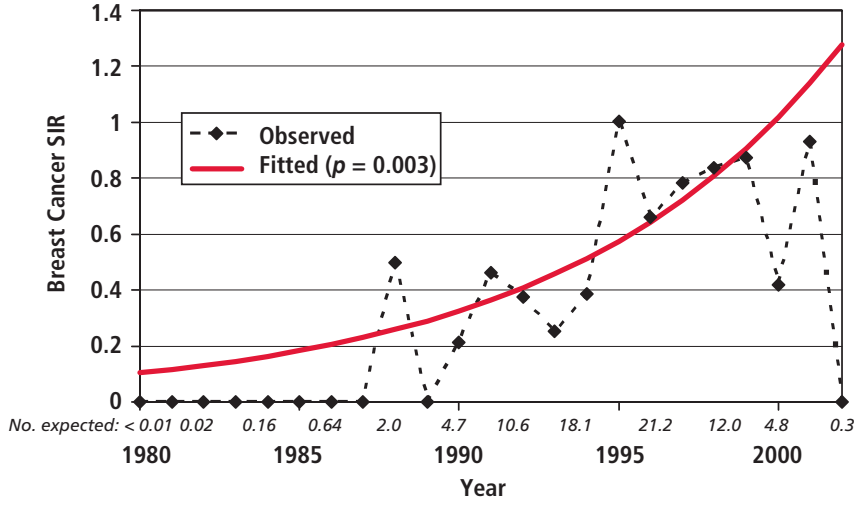


Figure 1. Observed and fitted standardized incidence ratios (SIRs) for breast cancer occurring one to five years after AIDS diagnosis. The number of expected cases is shown for even-numbered years. (Goedert JJ, et al. 2006)

(Detroit) (see Figure 2). Twenty-eight lung cancer patients (85%) and 69% of the cohort were smokers. After adjustment for smoking, risk remained elevated (SIR = 2.5; CI = 1.6–3.5), suggesting the involvement of additional factors. Incidence was unrelated to HIV-induced immunosuppression. **(Engels EA, Brock MV, Chen J, Hooker CM, Gillison M, Moore RD. Elevated incidence of lung cancer among HIV-infected individuals. *J Clin Oncol* 2006; 24:1383–1388)**

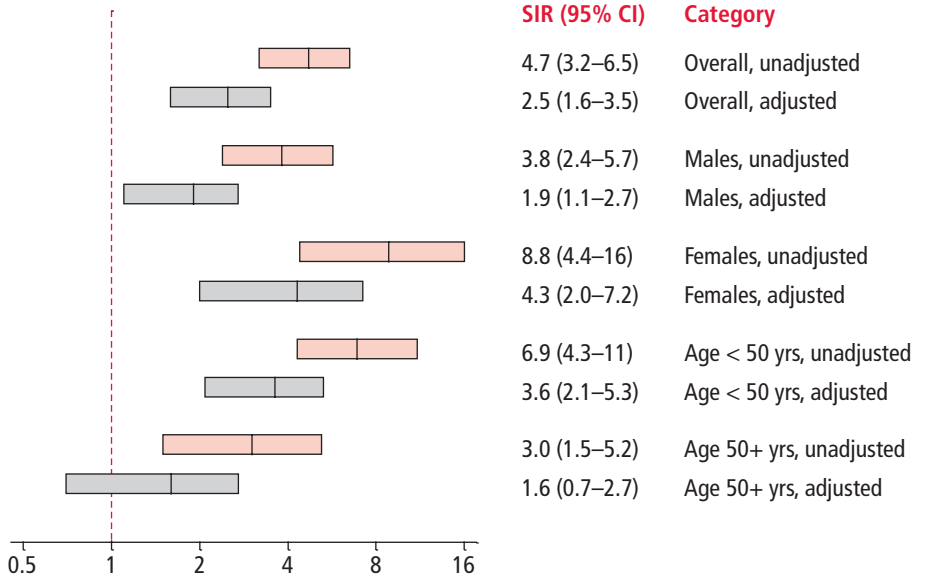


Figure 2. Standardized incidence ratios (SIRs) for lung cancer among HIV-infected patients relative to the Detroit general population, unadjusted and adjusted for smoking. (Engels EA, et al. 2006)

LIVER CANCER

DDT and DDE Exposures

To assess whether 1,1,1-trichloro-2,2-bis (p-chlorophenyl)ethane (DDT) and 1, 1-dichloro-2,2-bis(p-chlorophenyl) ethylene (DDE) are associated with hepatocarcinogenesis in humans, a nested case-control study was conducted among participants of the Nutritional Intervention Trials in Linxian, China. In a case group of 168 individuals who developed liver cancer during the trials and 385 controls, serum concentrations of DDT and DDE were measured by gas chromatography-mass spectrometry. The risk of developing liver cancer increased with increased serum DDT concentration (OR for quintile 5 vs. quintile 1 = 3.8; CI = 1.7–8.6; $p = 0.0024$) and was greater among individuals with DDE concentrations below the median value (OR for tertile 3 vs. tertile 1 = 3.55; CI = 1.45–8.74) than those with concentrations above the median (OR = 1.70; CI = 0.97–2.98). In contrast, there was no statistically significant association between liver cancer and serum DDE concentration. A calculation of crude liver cancer risk found that 26 liver cancers per 100,000 person-years were expected in the lowest quintile of DDT exposure vs. 46 liver cancers per 100,000 person-years in the highest quintile of DDT exposure. **(McGlynn KA, Abnet CC, Zhang M, Sun XD, Fan JH, O'Brien TR, Wei WQ, Ortiz-Conde BA, Dawsey SM, Weber JP, Taylor PR, Katki H, Mark SD, Qiao YL. Serum concentrations of 1,1,1-trichloro-2, 2-bis(p-chlorophenyl)ethane (DDT) and 1, 1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE) and risk of primary liver cancer. *J Natl Cancer Inst* 2006;98:1005–1010)**

LYMPHOMA

Immune Genes and NHL

Fifty-seven SNPs from 36 candidate immune genes were genotyped in 1,172 non-Hodgkin lymphoma (NHL) cases and 982 population-based controls from a U.S. multicenter study. A haplotype comprising SNPs in two proinflammatory cytokines, tumor necrosis factor–alpha and lymphotoxin-alpha (rs1800629, rs361525, rs1799724, rs909253, and rs2239704), increased NHL risk overall (OR = 1.31; CI = 1.06–1.63; $p = 0.01$) and notably for diffuse large B cell (OR = 1.64; CI = 1.23–2.19; $p = 0.0007$) (see Figure 3). A functional nonsynonymous SNP in the innate immune gene *Fcgamma receptor 2A* (*FCGR2A*; rs1801274) was also associated with NHL; AG and AA genotypes were associated with a 1.26-fold (CI = 1.01–1.56) and 1.41-fold (CI = 1.10–1.81) increased risk, respectively (p for trend = 0.006). Among NHL subtypes, the association with *FCGR2A* was pronounced for follicular and small lymphocytic lymphomas. **(Wang SS, Cerhan JR, Hartge P, Davis S, Cozen W, Severson RK, Chatterjee N, Yeager M, Chanock SJ, Rothman N. Common genetic variants in proinflammatory and other immuno-regulatory genes and risk for non-Hodgkin lymphoma. *Cancer Res* 2006;66:9771–9780)**

Waldenström Macroglobulinemia

A genome-wide linkage analysis was performed in 11 high-risk families with Waldenström macroglobulinemia (WM), for a total of 122 individuals with DNA samples, including 34 patients with WM and 10 with immunoglobulin M monoclonal gammopathy of undetermined significance (IgM MGUS). The authors genotyped 1,058

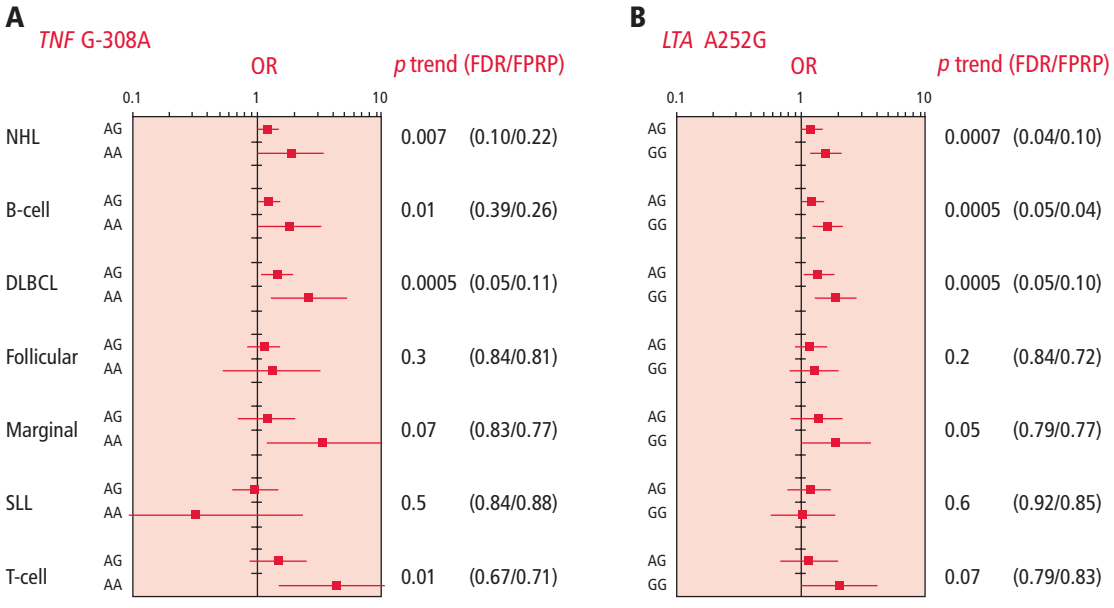


Figure 3. Association between *TNF* G-308A (A), *LTA* A252G (B), and non-Hodgkin lymphoma overall and by cell lineage and B-cell subtype. (Wang SS, et al. 2006)

microsatellite markers (average spacing 3.5 cM), performed nonparametric and parametric linkage analysis, and computed two-point and multipoint linkage statistics. The strongest evidence of linkage was found on chromosomes 1q and 4q when patients with WM and those with IgM MGUS were both considered affected; nonparametric linkage scores were 2.5 ($p = 0.0089$) and 3.1 ($p = 0.004$), respectively. Other locations suggestive of linkage were found on chromosomes 3 and 6. Findings from this first linkage analysis of families at high risk for WM represent important progress toward identifying gene(s) that modulate susceptibility to WM and understanding its complex etiology (see Figure 4). **(McMaster ML, Goldin LR, Bai Y, Ter-Minassian M, Boehringer S, Giambarresi TR, Vasquez LG, Tucker MA. Genomewide linkage screen for Waldenström macroglobulinemia susceptibility loci in high-risk families. *Am J Hum Genet* 2006; 79:695–701)**

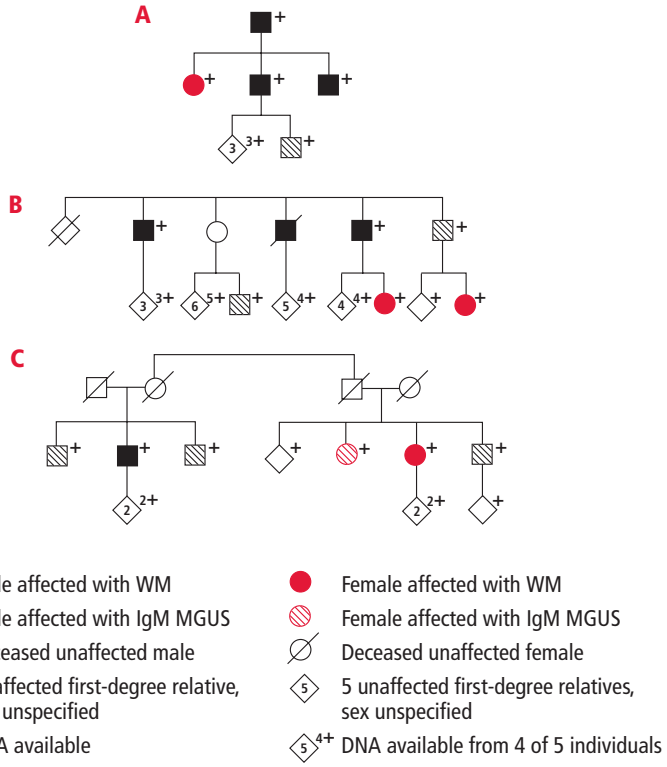


Figure 4. Examples of informative pedigrees, illustrating different pedigree structures among three study families. (McMaster ML, et al. 2006)

MELANOMA

Melanoma Susceptibility Genes

GenoMEL, comprising major familial melanoma research groups from North America, Europe, Asia, and Australia, has created the largest familial melanoma sample yet available to characterize mutations in the high-risk melanoma susceptibility genes *CDKN2A/alternate reading frames (ARF),* which encodes p16 and p14ARF, and *CDK4* and to evaluate their relationships with pancreatic cancer (PC), neural system tumors (NST), and uveal melanoma (UM). Among 466 families (2,137 patients) with at least three melanoma patients from 17 GenoMEL centers, 41% ($n = 190$) of families had mutations, most involving p16 ($n = 178$). Mutations in *CDK4* ($n = 5$) and *ARF* ($n = 7$) occurred at similar frequencies (2%–3%). There were striking differences in mutations across geographic locales. The proportion of families with the most frequent founder mutation(s) of each locale differed significantly across the seven regions included in the study ($p = 0.0009$). Single-founder *CDKN2A* mutations were predominant in Sweden (*p.R112_L113insR,* 92% of families' mutations) and the Netherlands (*c.225_243del19,* 90% of families' mutations). France, Spain, and Italy had the same most frequent mutation *(p.G101W)*. Similarly, Australia and the United Kingdom had the same most frequent mutations (*p.M53I, c.IVS2-105A>G, p.R24P,* and *p.L32P*). There was a strong association between PC and *CDKN2A* mutations ($p < 0.0001$), with differences by mutation. There was little evidence for an association between *CDKN2A* mutations and NST or UM. There was a marginally significant association between NST and *ARF* mutations ($p = 0.05$). **(Goldstein AM, Chan M, Harland M, Gillanders EM, Hayward NK, Avril MF, Azizi E, Bianchi-Scarra G, Bishop DT, Bressac-de Paillerets B, Bruno W, Calista D, Cannon Albright LA, Demenais F, Elder DE, Ghiorzo P, Gruis NA, Hansson J, Hogg D, Holland EA, Kanetsky PA, Kefford RF, Landi MT, Lang J, Leachman SA, Mackie RM, Magnusson V, Mann GJ, Niendorf K, Newton Bishop J, Palmer JM, Puig S, Puig-Butille JA, de Snoo FA, Stark M, Tsao H, Tucker MA, Whitaker L, Yakobson E; Melanoma Genetics Consortium (GenoMEL). High-risk melanoma susceptibility genes and pancreatic cancer, neural system tumors, and uveal melanoma across GenoMEL.** ***Cancer Res*** **2006;66:9818–9828)**

OSTEOSARCOMA

Perinatal Factors, Growth, and Development

In this study, osteosarcoma patients ($n = 158$) and controls with benign orthopedic conditions ($n = 141$) under age 40 were recruited from U.S. orthopedic surgery departments. Current height and age- and sex-specific height percentiles were not associated with osteosarcoma risk. Male cases, however, appeared to have an earlier adolescent growth period and earlier attainment of final height (OR = 7.1; CI = 1.6–50 for < 19 vs. ≥ 19 years), whereas earlier puberty appeared protective, with ORs of 0.41 (CI = 0.18–0.89) and 0.68 (CI = 0.31–1.5) for developing facial and pubic hair, respectively. High birth weight was associated with an elevated osteosarcoma risk (OR = 3.9; CI = 1.7–10 for 4,000 g vs. 3,000–3,500 g), although there was no trend in risk with increasing weight. These data provide some evidence that osteosarcoma is related to size at birth and in early adolescence, whereas earlier puberty in male subjects may be protective. **(Troisi R, Masters MN, Joshipura K, Douglass C, Cole BF, Hoover RN; the National Osteosarcoma Etiology Group. Perinatal factors, growth and development, and osteosarcoma risk.** ***Br J Cancer*** **2006;95:1603–1607)**

OVARIAN CANCER

Menopausal Hormone Therapy

The NIH-AARP Diet and Health Study Cohort included 97,638 women, aged 50–71 years at baseline, who completed two questionnaires (1995–1996 and 1996–1997). Incident ovarian cancers ($n = 214$) among these women through the year 2000 were identified with data from state cancer registries and mortality indices. Compared with no use of hormone therapy, use of unopposed estrogen for fewer than 10 years was not associated with ovarian cancer, while use for 10 or more years was associated with ovarian cancer among all women (relative risk [RR] = 1.89; CI = 1.22–2.95; $p = 0.004$) and, albeit not statistically significantly, among women with hysterectomy ($n = 19,359$; RR = 1.70; CI = 0.87–3.31; $p = 0.06$). Among the 73,483 women with intact uteri, 51,698 had used no hormone therapy or only estrogen plus progestin. Compared with no hormone therapy use, five or more years of use of sequential (progestin for < 15 days per cycle; RR = 3.09; CI = 1.68–5.68; $p < 0.001$) or continuous (progestin for ≥ 15 days per cycle; RR = 1.82; CI = 1.03–3.23; $p = 0.02$) estrogen plus progestin regimens were associated with ovarian cancer. Thus, long durations of use of unopposed estrogen and of estrogen plus progestin, especially sequential regimens, were associated with increased ovarian cancer risk. **(Lacey JV Jr, Brinton LA, Leitzmann MF, Mouw T, Hollenbeck A, Schatzkin A, Hartge P. Menopausal hormone therapy and ovarian cancer risk in the National Institutes of Health-AARP Diet and Health Study Cohort.** ***J Natl Cancer Inst*** **2006;98:1397–1405)**

PANCREATIC CANCER

Vitamin D Status

A prospective nested case-control study was conducted in the ATBC Cancer Prevention Cohort of male Finnish smokers, aged 50 to 69 years at baseline,

to test whether a higher vitamin D level, as determined by prediagnostic serum 25-hydroxyvitamin D [25(OH)D] concentrations, was associated with lower pancreatic cancer risk. Among 200 incident exocrine pancreatic cancer cases and 400 controls, higher vitamin D concentrations were associated with a threefold increased risk for pancreatic cancer (highest vs. lowest quintile, > 65.5 vs. < 32.0 nmol/L: OR = 2.92; CI = 1.56–5.48; $p = 0.001$) that remained after excluding cases diagnosed early during follow-up. Contrary to expectations, subjects with higher prediagnostic vitamin D status had a higher pancreatic cancer risk than those with lower status. **(Stolzenberg-Solomon RZ, Vieth R, Azad A, Pietinen P, Taylor PR, Virtamo J, Albanes D. A prospective nested case-control study of vitamin D status and pancreatic cancer risk in male smokers. *Cancer Res* 2006;66:10213–10219)**

PROSTATE CANCER

Vitamin E, Beta-carotene, and Vitamin C

The association between intake of micronutrient antioxidants and risk of prostate cancer was studied among men in the screening arm of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Among 29,361 men, including 1,338 prostate cancer cases occurring during follow-up, there was no overall association between prostate cancer risk and dietary or supplemental intake of vitamin E, beta-carotene, or vitamin C. However, among current and recent smokers, decreasing risks of advanced prostate cancer were associated with increasing dose (RR = 0.29; CI = 0.12–0.68; $p = 0.01$) and duration (RR for ≥ 10 years of use vs. none = 0.30; CI = 0.09–0.96; $p = 0.01$) of supplemental vitamin E use. Supplemental beta-carotene intake at a dose level of at least 2,000 µg/day was associated with decreased prostate cancer risk in men with low dietary beta-carotene intake (RR = 0.52; CI = 0.33–0.81). Among smokers, the age-adjusted rates of advanced prostate cancer were 492 per 100,000 person-years in those who did not take supplemental vitamin E, 153 per 100,000 person-years in those who took more than 400 IU/day of supplemental vitamin E, and 157 per 100,000 person-years in those who took supplemental vitamin E for 10 or more years. Among men with low dietary beta-carotene intake, the age-adjusted rates of prostate cancer were 1,122 per 100,000 person-years in those who did not take supplemental beta-carotene and 623 per 100,000 person-years in those who took at least 2,000 µg/day of supplemental beta-carotene. **(Kirsh VA, Hayes RB, Mayne ST, Chatterjee N, Subar AF, Dixon LB, Albanes D, Andriole GL, Urban DA, Peters U. Supplemental and dietary vitamin E, beta-carotene, and vitamin C intakes and prostate cancer risk. *J Natl Cancer Inst* 2006;98:245–254)**

SECOND CANCERS

Central Nervous System Cancers

A total of 116 subsequent primary neoplasms of the CNS occurred within a cohort of 14,361 five-year survivors of childhood cancers. Gliomas ($n = 40$) occurred a median of nine years after original diagnosis; for meningiomas ($n = 66$), the median was 17 years later. Radiation exposure was associated with increased risk of subsequent glioma (OR = 6.78; CI = 1.54–29.7) and meningioma (OR = 9.94; CI = 2.17–45.6). The dose response for the excess relative risk (ERR) was linear (for glioma, slope = 0.33, CI = 0.07–1.71 per Gray [Gy]; for meningioma, slope = 1.06, CI = 0.21–8.15 per Gy). For glioma, the ERR/Gy was highest among children exposed at less than five years of age. After adjustment for radiation dose, neither original cancer diagnosis nor chemotherapy was associated with risk. The overall SIR for glioma was 8.7, and the excess absolute risk was 19.3 per 10,000 person-years. **(Neglia JP, Robison LL, Stovall M, Liu Y, Packer RJ, Hammond S, Yasui Y, Kasper CE, Mertens AC, Donaldson SS, Meadows AT, Inskip PD. New primary neoplasms of the central nervous system in survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. *J Natl Cancer Inst* 2006;98:1528–1537)**

Sarcomas in Retinoblastoma Survivors

The risks for six subtypes of soft tissue sarcomas (fibrosarcoma, liposarcoma, histiocytoma, leiomyosarcoma, rhabdomyosarcoma, and "sarcomas not otherwise specified") were estimated in a cohort of 963 one-year survivors of hereditary retinoblastoma among patients diagnosed at two U.S. institutions from 1914 through 1984. SIRs were calculated for specific subtypes of soft tissue sarcomas by comparison with population data from the Connecticut Tumor Registry or the National Cancer Institute SEER database. Based on 69 soft tissue sarcomas in 68 patients, risks were elevated for soft tissue sarcomas overall (SIR = 184; CI = 143–233) and for individual subtypes. Leiomyosarcoma was the most frequent subtype (SIR = 390; CI = 247–585), with 78% of leiomyosarcomas diagnosed 30 or more years after the retinoblastoma diagnosis (SIR = 435; CI = 258–687). Among patients treated with radiotherapy for retinoblastoma, increased risks of soft tissue sarcomas were found in the field of radiation. Irradiated patients also had increased risks of soft tissue sarcomas, especially leiomyosarcomas, outside the field of radiation, and risks of soft tissue sarcomas were increased in nonirradiated patients as well. The cumulative risk for any soft tissue sarcoma 50 years after radiotherapy for retinoblastoma was 13.1% (CI = 9.7%–17.0%). **(Kleinerman RA, Tucker MA, Abramson DH, Seddon JM, Tarone RE, Fraumeni JF Jr. Risk of soft tissue sarcomas by individual subtype in survivors of hereditary retinoblastoma. *J Natl Cancer Inst* 2007;99:24–31)**

DCEG PEOPLE IN THE NEWS


Christian Abnet

Christian C. Abnet, Ph.D., M.P.H., Nutritional Epidemiology Branch (NEB), gave an invited talk on "The importance of selenium and zinc in esophageal cancer" at the Third Esophageal Cancer and Barrett's Metaplasia Research Summit in Las Vegas in November.

Between September and December, **Blanche P. Alter, M.D., M.P.H.,** Clinical Genetics Branch (CGB), spoke on Fanconi anemia as the Invited William Hathaway Professor at the University of Colorado Pediatric Hematology Retreat in Aspen, the Hematology Rounds at Johns Hopkins School of Medicine, Howard University Medical School, and the 18th Annual Fanconi Anemia Research Fund Scientific Symposium in Bethesda and on dyskeratosis congenita at the University of Minnesota Cancer Center Bone Marrow Transplant Conference in Minneapolis and the 48th Annual American Society of Hematology Meeting in Orlando.

Last fall, **William F. Anderson, M.D., M.P.H.,** Biostatistics Branch (BB), delivered talks on incidence and mortality data for subtypes of breast cancer at the annual SEER (Surveillance, Epidemiology, and End Results) meeting in Potomac, Maryland; at the National Naval Medical Center in Bethesda; at the Cancer Research Interest Group at George Washington University Medical Center; and at the annual Cancer Intervention and Surveillance Modeling Network breast cancer meeting in Bethesda.


Aaron Blair

In October, **Aaron Blair, Ph.D., M.P.H.,** Occupational and Environmental Epidemiology Branch (OEEB), gave invited talks entitled "Confounding and exposure misclassification in epidemiology: Discussion of the relative impact of each on estimates of relative risks in epidemiology studies" and "Formaldehyde and cancer: Scientific and public policy issues" at the Harvard School of Public Health; "Cancer and other diseases in the Agricultural Health Study" at Yale University; "Environmental epidemiology in understanding cancer etiology" at the Korean National Cancer Center in Seoul; and "Epidemiology studies of cancer in the Occupational and Environmental Epidemiology Branch of the National Cancer Institute" at Korea University in Seoul.


Louise Brinton

In December, **Louise A. Brinton, Ph.D.,** Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), spoke about "Long-term physical effects of ovulation stimulation" at the First World Congress on Natural Cycle/Minimal Stimulation IVF held in London.

Nilanjan Chatterjee, Ph.D. (BB), gave an invited talk on "Powerful linkage disequilibrium mapping by exploiting gene-gene and gene-environment interactions" to the Department of Biostatistics at Yale University in October.

Eric A. Engels, M.D., M.P.H., Viral Epidemiology Branch (VEB), gave an invited talk on "Simian virus 40 and human cancer" at the Keerti Shah Symposium at Johns Hopkins School of Public Health in October. He also gave two invited talks titled "Lung cancer in HIV-infected individuals" at the Department of Medicine of Miriam Hospital in Providence in October and at the Department of Medicine of the New England Medical Center in Boston in November.

In November, the Fifth Annual Gilbert W. Beebe Symposium, sponsored by the National Academies Nuclear and Radiation Studies Board, was held in Washington, DC. **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, delivered a talk titled "A tribute to the contributions of the pediatrician Robert W. Miller," and **Elaine Ron, Ph.D., M.P.H.,** Radiation Epidemiology Branch (REB), spoke about "Thyroid cancer in radiation-exposed children."

Mitchell H. Gail, M.D., Ph.D., Chief of BB, delivered a lecture titled "Absolute risk: Clinical applications and controversies" at George Washington University in October.


Neelam Giri

Neelam Giri, M.D. (CGB), presented "Immune function studies in Fanconi anemia" at the 18th Annual Fanconi Anemia Research Fund Scientific Symposium in Bethesda in October and "Immunoglobulin and lymphocyte subset abnormalities in patients with Fanconi anemia and

dyskeratosis congenita" at the 48th Annual American Society of Hematology Meeting in Orlando in December.


Gladys Glenn

Gladys M. Glenn, M.D. Ph.D., Genetic Epidemiology Branch (GEB), gave a keynote address on "Hereditary kidney cancer syndromes beyond von Hippel-Lindau (VHL)" at the Seventh International Symposium on VHL Disease and Hereditary Kidney Cancers in Ontario in October.

In September, **Lynn R. Goldin, Ph.D.** (GEB), delivered an invited talk on "Finding cancer susceptibility genes: Family and population approaches" as part of the 2006–2007 Distinguished Lecturers in Cancer Genetics Series at the Alvin J. Siteman Cancer Center at the Washington University Medical Center in St. Louis.

Harry Haverkos, M.D. (VEB), gave a talk on human immunodeficiency virus (HIV) as part of the Epidemiology and Control of Infectious Diseases Lecture Series at the Uniformed Services University of the Health Sciences in January.

In November, **Ann Hsing, Ph.D.** (HREB), gave invited talks on the molecular epidemiology of biliary tract and prostate cancers at the Seoul National University, the Korean National Cancer Center, and the Korean Genomics Society and on population-based prostate cancer studies at the Korean Urology Society, all in Seoul.

AACR CONFERENCE

At the Fifth Annual American Association for Cancer Research (AACR) Frontiers Conference in Boston in November, **Unhee Lim, Ph.D.** (NEB), received an AACR-AFLAC Scholar-in-Training Award for her abstract and poster presentation about "High genomic DNA methylation in leukocytes associated with low risk of colorectal adenoma among asymptomatic women" from the CONCeRN (Colorectal Neoplasia Screening with Coloscopy in Average-risk Women at Regional Naval Medical Centers) Study. Several other DCEG staff members presented talks at the conference:

- **Kenneth Adams, Ph.D.** (NEB): *Body mass and renal cell cancer incidence in a large U.S. cohort study*
- **Jiyoung Ahn, Ph.D.** (NEB): *Adiposity, adult weight change, and postmenopausal breast cancer risk*
- **Demetrius Albanes, M.D.** (NEB): *Serum vitamin E concentrations and prostate cancer risk in the PLCO Cancer Screening Trial*
- **Sanford M. Dawsey, M.D.** (NEB): *Chemoprevention of hepatocellular carcinoma: A randomized double-blind trial in Linxian, China*
- **D. Michal Freedman, Ph.D.** (REB): *Prospective study of serum vitamin D and cancer mortality in the United States*

AACR Conference Presenters: Philip Taylor, Traci Mouw, Rachael Stolzenberg-Solomon, Michael Leitzmann, Jiyoung Ahn, Yikyung Park, Margaret Wright, Behnoush Abedi, Sanford Dawsey, Farin Kamangar, D. Michal Freedman, Regina Ziegler, Unhee Lim, Jennifer Loud, Demetrius Albanes, and Larissa Korde. *(Photograph Credit: Sandra Rothschild)*

- **Farin Kamangar, M.D., M.P.H.** (NEB): *Ginseng intake and gastric cancer risk in the Shanghai Women's Health Study Cohort*
- **Larissa Korde, M.D., M.P.H.** (CGB): *Childhood soy intake and breast cancer risk in Asian American women*
- **Maria Teresa Landi, M.D., Ph.D.** (GEB): *Epidemiology and genetics: New results in melanoma etiology and their application to melanoma prevention*
- **Jennifer Loud, M.S.N., C.R.N.P.** (CGB): *Tolerability of breast duct lavage in women from BRCA mutation-positive families*
- **Yikyung Park, Sc.D.** (NEB): *Calcium intake and risk of cancer at multiple sites in the NIH-AARP Study*
- **Rachael Stolzenberg-Solomon, Ph.D.** (NEB): *Meat and meat-mutagen intake and pancreatic cancer in the NIH-AARP cohort*
- **Margaret Wright, Ph.D.** (NEB): *Genetic variation in the vitamin E transport pathway and risk of prostate cancer*

Larissa Korde, M.D., M.P.H. (CGB), presented "Gene expression profiling to predict response to neoadjuvant docetaxel and capecitabine for breast cancer" at the San Antonio Breast Cancer Symposium in December.

Ola Landgren, M.D., Ph.D. (GEB), gave the following invited talks: "On the pathway to multiple myeloma: Etiologic clues from familial and epidemiological studies" at the NIH metabolism meeting in September and "Patterns of immune stimulation and subsequent chronic lymphocytic leukemia (CLL): Etiologic clues from epidemiological studies in Europe and the United States" at the CLL Basic Research Program of the Feinstein Institute for Medical Research on Long Island in November.


Maria Teresa Landi

In September, **Maria Teresa Landi, M.D., Ph.D.** (GEB), gave a talk on "Molecular epidemiology of dioxin illness in Seveso" at the Joint International Society for Environmental Epidemiology and International Society of Exposure Analysis Conference on Environmental Epidemiology and Exposure in Paris and a keynote address on "Melanocortin-1 receptor gene and melanoma susceptibility" at the Pan-American Society for Pigment Cell Research in Cincinnati.

In September, **Sam Mbulaiteye, M.D.** (VEB), gave invited talks: "Applying record-linkage methods to study risks of cancers in people with HIV/AIDS in developing countries: The case of the Uganda HIV/AIDS Cancer Match Study" at the International Agency for Research on Cancer in Lyon, France and "Sero- and molecular epidemiology of human herpesvirus 8 infection in Uganda: The Uganda Sickle Cell HHV-8 Study" at the Uganda Virus Research Institute.


Katherine McGlynn

Katherine A. McGlynn, Ph.D. (HREB), spoke in October about "Trends in the incidence of testicular cancer by ethnicity in the United States" at the Sixth Copenhagen Workshop on Carcinoma *In Situ* of the Testis and Testicular Germ Cell Cancer, where she also cochaired a session on "Risk factors for testicular germ cell neoplasia."

June A. Peters, M.S., C.G.C. (CGB), presented "Familial testicular cancer: Survivors' and relatives' interest in genetic testing" at the Annual Education Meeting of the National Society of Genetic Counselors in Nashville; "The DNA damage response pathway, cancer susceptibility, and the public health" at the Annual American Society of Human Genetics Meeting in New Orleans; and "Humanizing health care: Medical family therapy for families with hereditary cancer" at the American Association of Marriage and Family Therapists in Austin.


Ruth Pfeiffer

In December, **Ruth Pfeiffer, Ph.D.** (BB), presented a seminar about statistical issues in genome-wide scans at the Laboratory of Neurogenetics of the National Institute on Aging.

Philip S. Rosenberg, Ph.D. (BB), delivered a talk titled "Genotype-phenotype associations in patients with severe congenital neutropenia" at the American Society of Hematology in Orlando in December.

Arthur Schatzkin, M.D., Dr.P.H., Chief of NEB, gave invited talks titled "Dietary fat and breast cancer: New life for an old hypothesis" at the Annual National Cancer Research Institute Conference in Birmingham and "A new partnership in biomedical and lifestyle research: The NIH-AARP Diet and Health Study" at AARP's National Event in Anaheim.

In December, **Steven L. Simon, Ph.D.** (REB), delivered an invited talk at the American Geophysical Union Conference in San Francisco on "Long-term consequences of radioactive fallout from conflicts involving nuclear explosions" in a special session titled Environmental Consequences of Regional Nuclear Conflicts.

Rachael Stolzenberg-Solomon, Ph.D. (NEB), gave presentations on the Pancreatic Cancer Cohort Consortium Whole Genome Scan (PanScan), a collaborative project of 13 studies that aims to identify genetic variants worth aggressive pursuit in population, clinical, and laboratory investigations, at NCI in December.

In September, **Mary H. Ward, Ph.D.** (OEEB), gave an invited talk on drinking water, nitrate, and health at the Department of Health Risk Analysis and Toxicology of the University of Maastricht in the Netherlands.

COMINGS . . . GOINGS

Andrew Bergen, Ph.D., has left the Genetic Epidemiology Branch (GEB) and taken a position as Program Director of Molecular Genetics at SRI International in Menlo Park, California, where he will focus on nicotine dependence, gene discovery, and translational research in clinical trials of smoking cessation.

Melinda Butsch Kovacic, Ph.D., M.P.H., a Division of Cancer Prevention Fellow with the Hormonal and Reproductive Epidemiology Branch (HREB) since 2002, has accepted a faculty position at Cincinnati Children's Hospital Medical Center in Cincinnati.

Shih-Chen Chang, Ph.D., has left the Nutritional Epidemiology Branch (NEB) for a position as an epidemiologist in the Discovery Medicine and Epidemiology Section of Research and Development at AstraZeneca Pharmaceutical Company, Inc., in Wilmington, Delaware.

Vladimir Drozdovitch, Ph.D., has joined the Radiation Epidemiology Branch (REB) as a visiting fellow. He has a doctorate in nuclear physics from the Institute of Power Engineering and Nuclear Research in Minsk, Belarus and has worked at the International Agency for Research on Cancer in Lyon, France, where he was responsible for the development and validation of dosimetric models and estimation of doses for the studies of cancer risk following the Chornobyl accident.


Vladimir Drozdovitch


Julia Gage

Julia Gage, M.P.H., became a predoctoral Cancer Research Training Fellow in HREB in September. For her dissertation research at Johns Hopkins University, she is working with **Mark Schiffman, M.D., M.P.H.,** and **Jose Jeronimo, M.D.,** to evaluate and improve visual diagnostic tools that detect cervical precancer.


Ying Gao

Ying Gao, M.D., Ph.D., has joined GEB as a visiting fellow. In 2006, she received her doctorate in nutritional sciences from Cornell University with minors in genetics, statistics, and epidemiology. Previously, she received an M.D. from Beijing Medical University and an M.P.H. from Peking University. During her fellowship with **Lynn R. Goldin, Ph.D.,** and **Philip R. Taylor, M.D., Sc.D.,** she will be working on linkage and association studies in cancer-prone families as well as case-control studies involving gene-environment interactions using data from the Esophageal Cancer Genetics Project.


Derek Hicks

Derek Hicks has joined the Occupational and Environmental Epidemiology Branch (OEEB) as a program assistant. During the last two years, he worked in the NIH Division of Extramural Activities Support and prior to that in the NIH National Center for Research Resources for four years. He received his B.B.A. in computer information systems from Baruch College, City University of New York in 1994.


Li Jiao

Li Jiao, M.D., Ph.D., has joined NEB as a postdoctoral fellow. In 2004, she obtained her Ph.D. in environmental sciences from the University of Texas Health Science Center at Houston School of Public Health. She worked at

In December, **Betsy Duane-Potocki** left DCEG for a position in the NCI Office of Management Analysis. She joined the Division in 1999 as its first Communications Coordinator. During her time at DCEG, she oversaw press contacts; media training; and responses to inquiries from the public, Congress, the Government Accountability Office, the Inspector General, and NIH General Counsel. She was particularly instrumental in coordinating audits and reviews of the Chornobyl Research Program. She also handled Freedom of Information Act requests, privacy issues, document clearance, and records management. She developed "Quick Reference Guides" on media contacts and various other topics, which have become useful tools across NCI. In 2004, Ms. Duane-Potocki received the DCEG Outstanding Mentoring Award in recognition of her mentoring of interns from the NCI Communications Intern Program and other programs.


Betsy Duane-Potocki

the M.D. Anderson Cancer Center for the past six years. Dr. Jiao will be working with **Rachael Stolzenberg-Solomon, Ph.D.,** on the role of nutritional and genetic factors in the etiology of pancreatic cancer.

Kimberly Kerstann, Ph.D., completed her GEB fellowship and has accepted a position with AstraZeneca as a Regional Scientific Manager.


Yan Li

Yan Li, Ph.D., has joined the Biostatistics Branch (BB) as a research fellow. She has master's degrees in animal genetics and breeding from the China Agricultural University and in statistics from the University of Nebraska–Lincoln, and she received her doctorate from the University of Maryland, College Park. She has worked in survey research at the National Center for Health Statistics and at Westat. During her fellowship in BB, Dr. Li will work on design-based and model-assisted methods for analyzing genetic data from the Third National Health and Nutrition Examination Survey and on developing statistical methods for epidemiologic analyses from complex samples.


Phuong Mai

Phuong Mai, M.D., has joined the Clinical Genetics Branch (CGB) as a staff clinician. She earned her medical degree from the University of Texas Medical Branch at Galveston and received training in internal medicine at Tulane University Medical Center and medical oncology at the University of Texas at San Antonio, where she also earned an M.S. in clinical investigation. Most recently, she completed a postdoctoral training program in clinical cancer genetics at the City of Hope National Medical Center in Duarte, California. Dr. Mai will be working with **Mark H. Greene, M.D.,** Chief of CGB, on the National Ovarian Cancer Prevention and Early Detection Trial.


Idan Menashe

Idan Menashe, Ph.D., has joined BB as a visiting fellow. In 2006, he received his doctorate in human genetics from the Weizmann Institute of Science in Israel. His dissertation research investigated the genetic basis of human olfactory variability. During his fellowship in BB, he will work on descriptive and analytical studies of cancer, including large-scale genetic association studies, with an emphasis on gene-environment interactions. **Philip S. Rosenberg, Ph.D.,** will serve as his primary mentor.

Evgenia Ostroumova, M.D., Ph.D., has joined REB as a postdoctoral fellow. She received an M.D. from the Chelyabinsk Medical Institute, Russia and a Ph.D. in internal medicine from the Tyumen Medical Academy, Russia. She worked in the epidemiology laboratory of the Urals Research Center for Radiation Medicine, where her primary research interest was the epidemiological study of health effects among rural residents in the Techa riverside who have been chronically exposed to ionizing radiation as a result of living in an area contaminated by a plant producing weapons-grade plutonium. During her fellowship, Dr. Ostroumova will work on the Chornobyl project with **Maureen Hatch, Ph.D., Elaine Ron, Ph.D., M.P.H.,** and **Alina Brenner, M.D., Ph.D.;** on the interventional fluoroscopist study with **Martha S. Linet, M.D., M.P.H.,** and **Ruth A. Kleinerman, M.P.H.;** and on the Techa River cohort study with Dr. Ron.


Evgenia Ostroumova


Roberto Minutillo (left) with Joseph Fraumeni

Roberto Minutillo left the DCEG Administrative Resource Center (ARC) in December to accept a promotion to Senior Administrative Officer at the National Institute of Arthritis and Musculoskeletal and Skin Diseases. He began his career with ARC as an intern in 1998 and became the administrative officer for REB in 1999.


Cristina Poscablo

Cristina Poscablo has joined OEEB as a predoctoral fellow. She is working toward her M.P.H. at George Washington University. She will work with **Lee Moore, Ph.D.,** on molecular and epigenetic studies of bladder cancer conducted in Argentina, Spain, and New England.

Cheryl Wagoner, M.A., served as an Administrative Career Development Intern in the Office of Division Operations and Analysis (ODOA) from September through December. She supported **Marianne K. Henderson, M.S.,** Chief of ODOA, with reporting and budget activities as well as **Kelli Langley** (ARC) on administrative officer activities.


Jessica Wilcox

Jessica Wilcox has joined ARC as an administrative technician. She has been with the federal government since 2001 and has worked for NIH, the U.S. Food and Drug Administration, and the Substance Abuse and Mental Health Services Administration. She is currently working on her bachelor's degree in business management from the University of Maryland University College. One of her main responsibilities will be review of travel authorizations and vouchers for the Office of the Director, CGB, HREB, and NEB.


Chu-ling Yu

Chu-ling Yu, Sc.D., has joined REB as a research fellow. In 2004, she received her doctorate in environmental health from the Harvard School of Public Health, where she continued her training as a postdoctoral fellow in molecular epidemiology. Her dissertation research examined the association between petrochemical exposures and the risk of leukemia and brain tumors with exposures assessed using geographic information systems. During her fellowship, she will evaluate carcinogenic risks of radiation, including interactions with genetic susceptibility. **André Bouville, Ph.D.,** and Ms. Kleinerman will serve as her mentors.

OEEB DISTINGUISHED LECTURER MARTYN SMITH SPEAKS AT DCEG


Nathaniel Rothman and Martyn Smith

Dr. Martyn T. Smith, Professor of Toxicology in the School of Public Health at the University of California, Berkeley visited NCI in November as a speaker for DCEG's Distinguished Lectures in Occupational and Environmental Cancer. A toxicologist well known for his outstanding contributions to the field of environmental and occupational molecular epidemiology, especially for increasing our understanding of the benzene toxicity mechanisms, Dr. Smith received his Ph.D. in biochemistry from St. Bartholomew's Hospital Medical College, London.

During his lecture on "Application of omic technologies in molecular cancer epidemiology," Dr. Smith underscored the value of the use of "omic" technologies, including genomics, silencing RNA libraries (small interfering RNA [siRNA]), transcriptomics (gene expression profiling), proteomics, and metabolomics, in molecular epidemiology. He noted that these technologies are evolving rapidly and continue to improve. Dr. Smith presented examples from collaborative projects he has carried out with investigators in DCEG, including studies of benzene and arsenic. He also discussed the rapidly emerging field of biosensor technology, which promises to greatly expand our ability to measure exposure to a wide range of compounds. He concluded, "These powerful new omic technologies, combined with good epidemiologic study design and robust statistical analysis, hold great potential for improving our understanding of cancer etiology."

During the two-day visit, Dr. Smith also met with investigators and fellows across the Division and gave a second seminar on future directions for studying occupational cancers to the members of the Occupational and Environmental Epidemiology Branch.

—Dalsu Baris, M.D., Ph.D.

INDOOR EMISSIONS FROM COAL COMBUSTION CAUSE CANCER

An International Agency for Research on Cancer (IARC) monograph working group has concluded that indoor emissions from household combustion of coal are Group 1 carcinogens in humans, associated primarily with an increased risk of lung cancer. **Qing Lan, M.D., Ph.D., M.P.H.,** an investigator in the Occupational and Environmental Epidemiology Branch (OEEB), was a member of the working group, and her research in Xuanwei County, Yunnan Province, China, served as the primary evidence.

Other DCEG scientists also contributed to the research leading to these conclusions. In the late 1980s, DCEG Director **Joseph Fraumeni, Jr., M.D.,** and colleagues carried out a case-control study in Shenyang, Liaoning Province, China, and found that indoor exposure to coal smoke was associated with increased lung cancer risk.

The IARC working group also concluded that indoor emissions from household combustion of biomass fuel (mostly wood) and from high-temperature frying (stir-frying, deep-frying, and pan-frying) are probably carcinogenic (Group 2A category) in humans. Biomass fuel is much more widely used in Chinese households than coal, although this varies by region.

Exposure to environmental carcinogens varies widely across the continents, but the use of solid fuels for cooking and heating is most common in low- and medium-resource countries, where about half the world's population lives. Risk may be greatest for women and children, who spend more time at home. "This provides a warning that exposure to indoor combustion of coal and biomass fuels is hazardous and that steps need to be taken to reduce such exposure, for example, improving indoor ventilation," said Dr. Lan, pointing out that millions of people are at increased risk from such indoor air pollution around the world. In fact, a study she carried out showed that improved venting of indoor combustion products resulted in a drop in lung cancer rates.

In China, coal is often used as fuel for cooking fires, which exposes many families to dangerous indoor air pollution.

The working group, comprising 19 scientists from eight countries, was convened by the IARC Monographs Programme. Based in Lyon, France, IARC is the cancer research agency of the World Health Organization. A summary of their evaluation was published in the December issue of *Lancet Oncology;* the results were also presented at the annual meeting of the Society for Risk Analysis in Baltimore on December 4. ■

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