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DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS

Linkage

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U.S. Military Cancer Institute Collaboration Offers Special Research Opportunities

After more than two years of strategic planning, a collaboration between DCEG and the U.S. Military Cancer Institute (USMCI) is under way that could change what we know about the epidemiology of cancer.

Analyzing data on more than 9 million active and retired military personnel and their families, researchers will estimate cancer incidence and mortality rates in the military and study the effects of medical history, medication use, and occupational and other exposures on cancer risk. The wealth of information—including more than 31 million serum samples—will allow studies of unprecedented scope and strength, particularly for research on uncommon cancers, cancers common among young people (such as lymphoma and testicular cancer), and cancers that occur more frequently in minority populations.

"The importance of the collaboration with USMCI cannot be overstated," said **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director and member of USMCI's Scientific Advisory Board. "It is clear that the prospects for innovative epidemiologic research are enormous in light of the unique resources within the military health system."

NCI–USMCI Collaborators: (front) Kangmin Zhu and Joseph Fraumeni; (back) Shelia Zahm and Robert Hoover.

Established in 2001, USMCI has a mandate from Congress to reduce the burden of cancer in the military. With headquarters at Walter Reed Army Medical Center in Washington, DC, USMCI is a component of the Uniformed Services University of the Health Sciences, led by Dr. Charles Rice. Dr. William Winkenwerder, the Assistant Secretary of Defense for Health Affairs, recently designated USMCI to lead Department of Defense (DoD) research efforts in cancer epidemiology.

Dr. John F. Potter, Director of USMCI, established its Epidemiology Program to capitalize on the extraordinary resources available across DoD. Dr. Kangmin Zhu, USMCI's

DCEG *Linkage*

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Associate Director for Epidemiology and an adjunct investigator in DCEG, has worked diligently to start the collaboration. Due to the number of organizations included within DoD, obtaining the administrative, scientific, and human research ethics approvals has been a daunting task, but the research team is now beginning to acquire and analyze data that will identify the magnitude of the cancer burden in the military population.

As a first step, Dr. Zhu created a detailed inventory of military-based resources. These include data on diagnosis, treatment, prescription history, inpatient and outpatient visits, as well as deployment, occupation, and demographic information on more than 9.5 million beneficiaries. DoD also has a repository of serum samples collected after 1990 from active-duty and reserve military personnel. Typically, serum samples are collected at the time of entry into the military and every one to two years thereafter. About 2.3 million specimens are added each year to the repository, which now has more than 31 million samples. At least one pre-diagnostic serum sample is available for more than 80 percent of the cancer patients whose clinical information is in the DoD databases.

"These pre-diagnostic specimens are precious for biomarker research into the etiology and early detection of cancer," Dr. Zhu emphasized. "The databases and serum repository provide a unique opportunity for state-of-the-art research." Thinking about the sheer amount of data and the potential for research protocols is a kid-in-a-candy-store moment for any cancer epidemiologist.

"The U.S. military health system is basically the largest health maintenance organization in the country," said **Shelia Hoar Zahm, Sc.D.,** DCEG Deputy Director and a principal investigator on the collaborative project. "The large population and computerized health databases are an amazing resource. The DoD serum samples are incredibly valuable, because they can be tapped for special studies in viral epidemiology, metabolic profiles, and proteomics."

The diversity of the military population is an important feature that could lead to new insights into cancer risk. "Most of the existing general population cohorts are primarily Caucasian and middle to upper class," Dr. Zahm said. "So this is a great population to test whether information from other studies holds true among minorities and other socioeconomic groups, and to explore reasons for the racial and ethnic disparities in cancer incidence."

An external advisory panel of scientists was created to counsel and guide USMCI's Epidemiology Program, providing input on the strategic plan and how best to prioritize research topics and establish collaborations. **Robert Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, serves as the group's Chair.

An immediate goal of the USMCI/NCI research program is to conduct record-linkage studies that will both describe the burden of cancer in the military and look at possible associations between cancer and certain exposures. "Currently, we're looking at huge databases that have issues of comparability, completeness, and accuracy," said **Susan Devesa, Ph.D.,** a senior investigator in the Biostatistics Branch (BB). "We're trying to pull them together, consolidate them, and produce summary records."

"The descriptive information is important for DoD and also provides valuable pointers for further research," Dr. Zhu

added. "We are now ready to explore some specific research questions using the databases." For example, **Ola Landgren, M.D., Ph.D.,** a research fellow in the Genetic Epidemiology Branch, plans to look at reasons for the racial and ethnic differences in the incidence of multiple myeloma, which occurs at higher rates in the black population. As part of the project, he will utilize the serum repository to examine patterns of monoclonal gammopathy of undetermined significance, which appears to be a precursor to multiple myeloma.

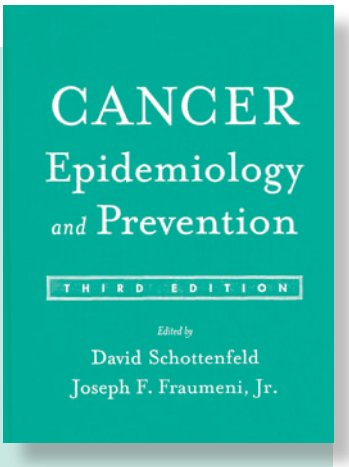
In addition, **Michael Leitzmann, M.D., Dr.P.H.,** a tenure-track investigator in the Nutritional Epidemiology Branch, will explore associations between physical activity levels and various forms of cancer, as well as conduct studies linking markers of chronic inflammation to the risk of prostate cancer, again using pre-diagnostic serum samples. "We hypothesize that chronic inflammation is positively associated with prostate cancer risk," he said. "We will also be able to determine whether the association is more pronounced in men with increased insulin resistance or is modified by circulating levels of testosterone."

"The large population and computerized health databases are an amazing resource. The DoD serum samples are incredibly valuable, because they can be tapped for special studies in viral epidemiology, metabolic profiles, and proteomics."

A joint USMCI/NCI Steering Committee will oversee the collaboration. Committee members from NCI include Drs. Zahm and Devesa along with **William Anderson, M.D., M.P.H.** (BB); **Eric Engels, M.D., M.P.H.** (Viral Epidemiology Branch); **Katherine McGlynn, Ph.D., M.P.H.** (Hormonal and Reproductive Epidemiology Branch); and **Philip Rosenberg, Ph.D.** (BB). Committee members from USMCI include Drs. Zhu, Ismail Jatoi, Tzu-Cheg Kao, Jennifer Rusiecki, and Hongyu Wu. Along with the external advisory panel, this group will help identify the most compelling research questions that can be uniquely addressed through epidemiologic research in the military population. ■

—Nancy Volkers

DIVISION DIRECTOR UPDATES TEXTBOOK



The third edition of *Cancer Epidemiology and Prevention,* edited by Dr. David Schottenfeld (University of Michigan), and **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, was recently published. This definitive reference volume has been a valuable resource for epidemiologists, oncologists, and other scientists since its first publication in 1982. The new edition gives special emphasis to the integration of epidemiologic methods with genomic and other emerging technologies that provide new insights into the role of genetic predisposition and gene-environment interactions in cancer etiology.

The 72-chapter volume provides a comprehensive overview of cancer epidemiology in five sections: Basic concepts, The magnitude of cancer, The causes of cancer, Cancer by tissue of origin, and Cancer prevention and control. The edition also includes new chapters on social class disparities in cancer incidence and mortality, the role of obesity and physical inactivity in cancer etiology, the potential effects of electromagnetic fields and radiofrequency radiation, and principles of cancer chemoprevention.

Associate Editors Dr. Jonathan Samet (Johns Hopkins University), Dr. Graham Colditz (Harvard University), and Dr. Alice Whittemore (Stanford University) also contributed to the new edition, as did several DCEG scientists: Dalsu Baris, M.D., Ph.D., Kenneth Cantor, Ph.D., Neil Caporaso, M.D., Rochelle Curtis, M.A., Kim Danforth, Sc.D., Susan Devesa, Ph.D., Montserrat Garcia-Closas, M.D., Dr.P.H., Mark Greene, M.D., Patricia Hartge, Sc.D., Allan Hildesheim, Ph.D., Ann Hsing, Ph.D., James Lacey, Jr., Ph.D., Martha Linet, M.D., M.P.H., Jay Lubin, Ph.D., Katherine McGlynn, Ph.D., Robert W. Miller, M.D., Lee Moore, Ph.D., Charles Rabkin, M.D., Elaine Ron, Ph.D., Nathaniel Rothman, M.D., M.P.H., M.H.S., Mark Schiffman, M.D., M.P.H., Mark Sherman, M.D., Debra Silverman, Sc.D., Sophia Wang, Ph.D., and Mary Ward, Ph.D.

—Catherine McClave, M.S.

JORGE TORO EXPLORES HEREDITARY SKIN DISEASES

Would it be a bit too clever to say that research conducted by **Jorge R. Toro, M.D.,** a tenure-track investigator and dermatologist in the Genetic Epidemiology Branch (GEB), has gotten under his skin? Perhaps. But Dr. Toro clearly loves what he studies: inherited skin diseases and their associations with kidney cancer.

For nearly a decade, Dr. Toro has been studying families with Birt-Hogg-Dubé syndrome (BHDS), an autosomal dominant condition that involves small skin papules (called fibrofolliculomas) on the scalp, face, and neck. In some cases, BHDS also involves episodes of spontaneous pneumothorax (or collapsed lung) and/or multiple or bilateral renal cell carcinomas. Most people are first diagnosed with BHDS by skin findings. Subsequently, a screening of the kidneys may reveal renal cell cancer.

After describing the association of BHDS with kidney cancer, Dr. Toro worked with Dr. Berton Zbar and Dr. Marston Linehan from NCI's Urologic Oncology Branch (UOB) in the Center for Cancer Research to map and clone the gene responsible for the syndrome. Dr. Toro is now researching how spontaneous pneumothorax relates to the syndrome.

In a 2003 publication, Dr. Toro and colleagues in UOB described the first group of North American families with another genetic skin disease, or genodermatosis, that confers an increased risk of kidney cancer called hereditary leiomyomatosis and renal cell cancer (HLRCC). "Here at NCI, we have the largest cohort of patients in the world with HLRCC and the largest cohort reported with kidney cancer," said Dr. Toro.

Dr. Toro with **Gladys Glenn, M.D., Ph.D., Laveta Stewart, M.P.H.,** and others in GEB recently completed a nested case-control study to investigate the risk of uterine fibroids among women with HLRCC. They also published a review article on HLRCC that was selected for continuing medical education credits in the *Dermatology Nursing Journal*.

People with HLRCC have a germline mutation in the gene coding for fumarate hydratase (FH), an enzyme in the energy-generating Krebs cycle. "We've found significantly decreased FH enzyme activity in cells from patients with HLRCC," Dr. Toro said. "Some patients with HLRCC have enzyme activity as low as people with fumarate hydratase deficiency," another inherited condition, usually fatal, in which people have mutations in both *FH* genes. Dr. Toro's laboratory research team, including Dr. Manop Pithukpakorn (National Human Genome Research Institute), Dr. Ming Wei (SAIC), and **Ousmane Toure, Ph.D.** (GEB), just published this finding in the *Journal of Medical Genetics*.


Jorge Toro

Dr. Toro and others constructed a homology model of human FH to investigate if the location of the mutations might provide clues to functional problems. "We were interested in looking at connections to kidney cancer, but we could not find a correlation between altered functionality and tumorigenesis," he said. "But I believe that what leads to cancer is more complex than just an amino acid change in an enzyme."

In a project funded by an NCI Director's Intramural Innovation Award, Dr. Toro is identifying and validating a novel protein that binds FH. This research will help to elucidate how FH interacts with other proteins and to identify novel pathways involved in tumorigenesis. A knockout mouse model is in the works.

Since his childhood in Puerto Rico, Dr. Toro had plans for medical school. In the mid-1980s, he traveled to western New York to attend Cornell University. To keep warm, he wore a coat that "went down to my ankles." Undeterred by the cold winters, Dr. Toro received his medical degree with honors from the State University of New York at Buffalo. He published his first dermatology paper, on the topic of "Prognostic factors and evaluation of mycosis fungoides and Sézary syndrome," nine years ago in the *Journal of the American Academy of Dermatology* using data he collected at the Roswell Park Cancer Institute.


Experts from around the world participated at the Workshop on Hereditary Leiomyomatosis and Renal Cell Carcinoma. *(Photograph Credit: Bill Branson)*

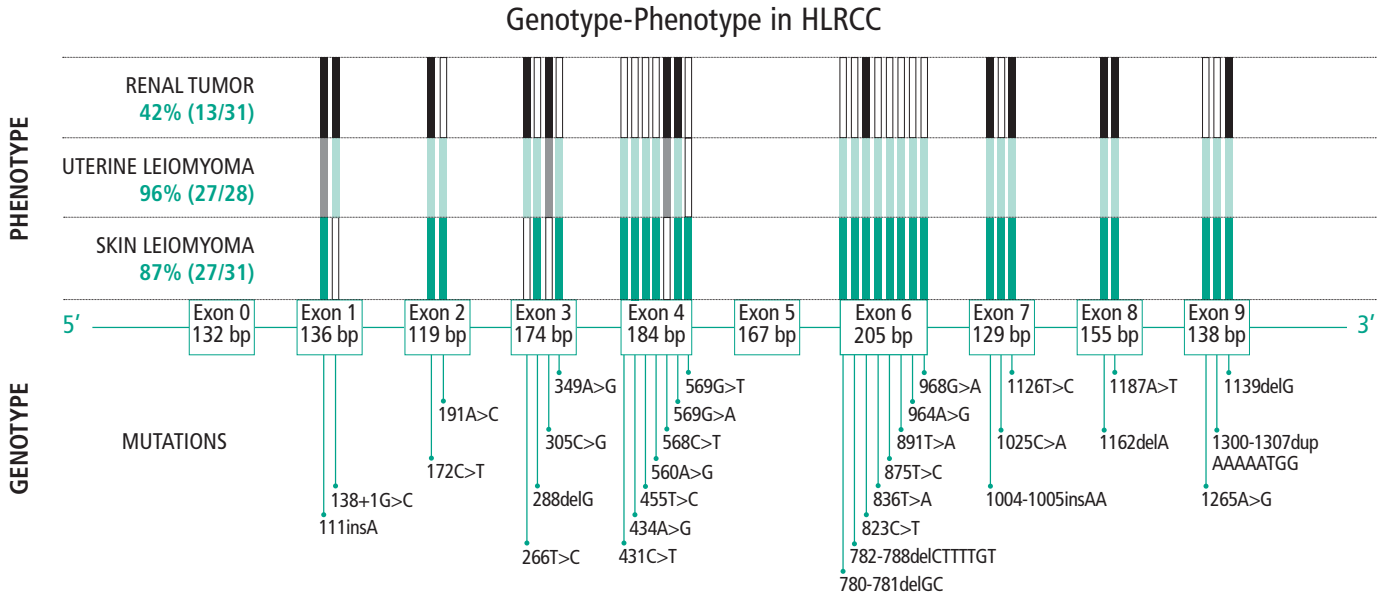


Figure 1. Distribution of *FH* mutations and the genotype-phenotype in HLRCC. The lower vertical arrows denote *FH* mutations. The upper vertical bars show the phenotype corresponding to the specific *FH* mutation. The colors in the vertical bars indicate the phenotype: black, renal tumor; pale green, uterine fibroid; and bright green, skin leiomyoma. The empty bars indicate the absence of phenotype and the gray bars denote unknown phenotype status. (Wei M-H, et al. *J Med Genet;* 43:18–27; 2006)

Though the decision to be a physician was easy, deciding on a specialty was not. Dermatology has proven a great fit for both Dr. Toro's visual mode of thinking and his love of pathology.

"I thought it was interesting that I didn't have to use an x-ray or fancy tests for a diagnosis—I can just examine the skin of the person," he said. "The skin gives you lots of clues for making diagnoses of internal conditions as well. But I also perform a skin biopsy and analyze it under the microscope, so I use a lot of pathology."

Here in DCEG, Dr. Toro is intrigued by population studies. "What I'm attempting to do now is to take the findings from the family-based studies and investigate how they apply to the general population," he said. "How do the genes (*BHD* and *FH*) we identified in familial kidney cancer play a role in sporadic kidney cancer?" Dr. Toro is screening renal tumors from case-control studies conducted in Eastern Europe and in the United States for mutations in *BHD* and *FH* to investigate the role they may play in kidney cancer in large populations.

This past July, he and colleagues discussed their research at a workshop on HLRCC chaired by Dr. Toro and cosponsored by NIH's Office of Rare Diseases. Goals of the workshop were to describe existing research, develop provisional diagnostic criteria, formulate recommendations for research and surveillance of high-risk families, and identify potential collaborations and future research questions. Participants included Dr. Glenn and Ms. Stewart; Dr. Virpi Launonen, University of Helsinki; Dr. Ian Tomlinson, London Research Institute; Dr. Gary Chuang, Boston Medical Center; Dr. Constantine Stratakis, National Institute of Child Health and Human Development; Dr. Elaine Ostrander, National Human Genome Research Institute; Dr. Stan Lilleberg, Transgenomic, Inc.; and others from NCI, academic institutions, industry, and the HLRCC Family Alliance. A summary of the proceedings is being developed for publication.

Dr. Toro is first author on a paper for an upcoming issue of the *International Journal of Cancer* that uses SEER data to describe the epidemiology of soft-tissue sarcomas in the United States. The group found that 40 percent of leiomyosarcomas in women were of uterine origin. "A few reports suggest that women with HLRCC may be more susceptible to getting leiomyosarcomas of the uterus," Dr. Toro said. "We know there are inherited conditions that predispose to sarcomas. Now we can investigate sarcomas in the general population and compare them at the clinical and molecular level."

In future research, Dr. Toro would like to find genes responsible for other genodermatoses and investigate how this knowledge might provide clues to cancer etiology and biology.

"I think we have a good approach to study the causes of disease," he concluded. "I would like to increase efforts in searching for new genes in familial cancer syndromes and investigating how they apply to cancer in the general population. I think this is a good model to study other types of cancer. We learn from the families, and then apply that knowledge to cancer and even to other diseases." ■

—Nancy Volkers

MEMBERS PARTICIPATE IN CONGRESS OF EPIDEMIOLOGY

Epidemiologists from around the world gathered at the Second North American Congress of Epidemiology in Seattle this past June. The 2006 Congress was cosponsored by 19 national and international organizations that share a focus on epidemiology, including the American College of Epidemiology (ACE), the American Public Health Association (APHA), the Canadian Society for Epidemiology and Biostatistics, and the Society for Epidemiologic Research (SER). Plenary sessions addressed both the breadth and depth of epidemiology, including presentations on cervical cancer control as a model for recognizing and solving public health problems, use of epidemiology in the courtroom, and population health as a criterion for sustainability. In addition, each organization presented a symposium reflecting its area of research. The Congress agenda covered more than 1,000 events, including poster presentations, pre-meeting workshops, and special events for students.

Many staff from DCEG played leadership roles at the Congress. **Martha Linet, M.D., M.P.H.,** Chief of the Radiation Epidemiology Branch (REB) and a past president of ACE, and **Maureen Hatch, Ph.D.,** head of the Chornobyl Research Unit in REB and a past president of SER, served on the Program Committee and cochaired a symposium on high-yield cancer data from low-dose radiation exposures. Dr. Hatch's presentation at the symposium was titled "Thyroid cancer and related disorders in young persons residing in regions contaminated by the Chornobyl accident." **Elaine Ron, Ph.D.,** another senior investigator in REB, spoke on cancer risks associated with medical radiation exposures, which was quoted in the August issue of *JAMA*. The symposium also included a presentation about risks faced by nuclear workers.

Louise Brinton, Ph.D., Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), led a roundtable entitled "Hormones and cancer risk: Why are there so many unresolved issues?" and chaired a spotlight session, "Unresolved issues regarding exogenous hormones and cancer risk." At the spotlight session, **James Lacey, Ph.D.,** a tenure-track investigator in HREB, spoke on "Endometrial cancer and menopausal estrogen-plus-progestin therapy: A cohort study." At a symposium on the design and analysis of case-control and case-cohort studies, **Nilanjan Chatterjee, Ph.D.,** a senior investigator in the Biostatistics Branch (BB), presented a lecture entitled "Analysis of case-control studies in genetic epidemiology: Classic logistic regression and some novel alternatives." At a symposium on Clusters, Infections, and Childhood Cancer, **James Goedert, M.D.,** Chief of the Viral Epidemiology Branch (VEB), gave a talk on the association between infection and cancer, emphasizing childhood leukemia. In the plenary session, Recognizing and Solving Public Health Problems with Epidemiology: The Example of Cervical Cancer Control, **Allan Hildesheim, Ph.D.,** a senior investigator in HREB, presented "Molecular epidemiology of cervical cancer: The road from etiologic understanding to preventive strategies."

At a symposium on Assessing Ethnicity in Populations, **Sholom Wacholder, Ph.D.,** a senior investigator in BB, spoke on population stratification in genetic association studies. Along with Dr. Jonathan Samet of Johns Hopkins University, Dr. Wacholder organized a symposium entitled Growth of Multicenter, Multidisciplinary, Multi-investigator Studies: How Is "Big" Epidemiology Changing Epidemiology? **Robert Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program (EBP), addressed "The evolution of epidemiologic research: From 'cottage industry' to 'big science'" at this symposium. At a session devoted to occupational epidemiology, **Preetha Rajaraman, Ph.D.,** a postdoctoral fellow

Left: Robert Hoover and Patricia Hartge received honors at the 2006 Congress. Right: Ruth Kleinerman received 2nd place prize for her poster. *(Photograph credit: Sandra Rothschild)*

in REB, presented a lecture on lead exposure, genetic susceptibility, and the risk of adult brain tumors.

Twenty-five DCEG members presented posters reporting their research on topics ranging from nutrition, hormones, occupational exposures, infectious agents, genetics, radiation, tobacco use, and descriptive data. **Sandra Rothschild,** Office of the Director, manned the DCEG exhibit and recruitment booth.

Several DCEG members received awards and honors at the Congress. **Patricia Hartge, Sc.D.,** Deputy Director of EBP, received the Distinguished Epidemiologist Award, which is given jointly by SER, APHA, and ACE. It is awarded every five years to honor major accomplishments and contributions to the field of epidemiology. **Ruth Kleinerman, M.P.H.,** a staff scientist in REB, won second prize at the Congress for her poster entitled "Improving questionnaire-based assessment of ultraviolet radiation from sunlight: Agreement between daily diary and recalled time outdoors six months later." DCEG coauthors included **Gabriel Chodick, Ph.D.** (REB), **D. Michal Freedman, Ph.D.** (REB), **Thomas Fears, Ph.D.** (BB), and Dr. Linet.

Gabriella Andreotti, M.P.H., and **Kelly Yu, M.P.H.,** predoctoral fellows in HREB, were among 11 students selected in a national competition to participate in the SER Student Workshop on methodologic issues.

Finally, because the 2005 ACE meeting in New Orleans was cancelled following Hurricane Katrina, recipients of last year's ACE awards, including the 22nd Lilienfeld Award winner, Dr. Hoover, were feted at a special "Enjoy and Learn" reception. Dr. Hoover was honored for being one of the nation's leading cancer epidemiologists. ■

NIH RECOGNIZES 2007 FARE WINNERS

The NIH Fellows Award for Research Excellence (FARE) program recognizes outstanding scientific research by intramural postdoctoral fellows. Fellows submit abstracts of their research, which are reviewed by a panel of NIH postdoctoral fellows and tenured/tenure-track investigators. In 2007, the FARE program was sponsored at the NIH level by the Scientific Directors, Office of Intramural Training and Education, Office of Research on Women's Health, and Fellows Committee. Only 25 percent of the applicants receive awards. Winners receive a $1,000 travel stipend to attend and present their work at a scientific meeting in the United States. This year, nine DCEG fellows received awards. More information about the FARE competition is available at http://felcom.nih.gov/FARE.

FARE Winners: (front) Aimee Kreimer, Mahboobeh Safaeian, and Unhee Lim; (back) Jonine Figueroa, Lindsay Morton, Rajeev Mahajan, Parveen Bhatti, Anil Chaturvedi, and Sonja Berndt.

DCEG FARE Winners and Abstract Titles

- **Sonja Berndt, Pharm.D., Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB): *Disparities in survival between black and white patients with renal cell cancer*
- **Parveen Bhatti, Ph.D.,** Radiation Epidemiology Branch (REB): *DNA double-strand break repair polymorphisms, ionizing radiation exposure, and breast cancer risk*
- **Anil Chaturvedi, Ph.D.,** Viral Epidemiology Branch (VEB): *Elevated risk of lung cancer among people with AIDS*
- **Jonine Figueroa, Ph.D., M.P.H.,** Hormonal and Reproductive Epidemiology Branch (HREB): *Evaluation of genetic variation in the double-strand break repair pathway suggests an association with bladder cancer risk*
- **Aimee Kreimer, Ph.D.** (HREB): *HPV testing following loop electrosurgical excision procedure (LEEP) identifies women at risk for post-treatment cervical intraepithelial neoplasia grade 2 or 3 disease*
- **Unhee Lim, Ph.D.,** Nutritional Epidemiology Branch (NEB): *Gene-nutrient interactions in one-carbon metabolism and the risk of non-Hodgkin lymphoma: NCI-SEER case-control study (1998–2000)*
- **Rajeev Mahajan, M.H.S.** (OEEB): *Fonofos exposure and cancer incidence in the Agricultural Health Study*
- **Lindsay Morton, Ph.D.** (HREB): *Hepatitis C virus (HCV) infection and risk of post-transplant lymphoproliferative disorder (PTLD) after liver transplantation*
- **Mahboobeh Safaeian, Ph.D.** (HREB): *Utility of self-collected vaginal swabs for studying the epidemiology of carcinogenic human papillomavirus (HPV) infections: Determinants of incidence and clearance of carcinogenic HPV in Rakai, Uganda*

DOSIMETRY MONOGRAPH PUBLISHED

Members of the Radiation Epidemiology Branch (REB) recently published a monograph, *Uses of Dosimetry in Radiation Epidemiology*, as a special supplement to the journal *Radiation Research*. The monograph introduces readers to an array of dosimetric methods and applications that have been used to reconstruct radiation exposures for epidemiologic studies. Most of these studies have required reconstructing doses many years after the exposures have taken place. Because appropriate data are rarely available, researchers in radiation dosimetry have developed a variety of innovative strategies that combine historical data, often limited in quantity and quality, with the most appropriate models.

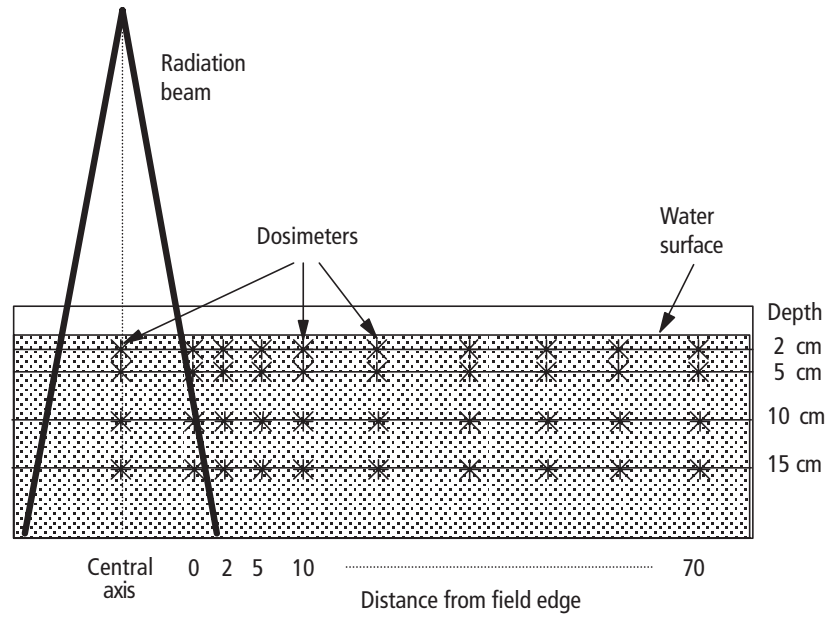
This monograph fills a void in the technical literature by describing radiation dosimetry methods in terms understandable to epidemiologists, dosimetrists, and statisticians. The collection of 12 papers coauthored by 60 international dosimetry and epidemiology experts describes a wide range of methods and their applications.

The monograph includes discussions about dosimetry methods for assessing exposures of many types including those from medical radiation, radioactive fallout from nuclear testing, radioactivity releases from the Chornobyl accident, and occupational exposures including exposure to radon. Papers that address measurements of biological samples to estimate dose (i.e., biodosimetry) and statistical methods to evaluate and account for uncertainty are also included. One of the latest articles describes in detail the most recent revision of methods used to estimate doses received by survivors of the World War II detonations of atomic bombs in Japan.

The monograph is especially timely given today's concerns about nuclear accidents and acts of radiological terrorism.

The monograph was produced by a REB working group chaired by **Steven Simon, Ph.D.,** and including Branch members **André Bouville, Ph.D., Ruth Kleinerman, M.P.H.,** and **Elaine Ron, Ph.D.,** with administrative support from **Kathleen Stine, M.B.A.** All papers were peer-reviewed and can be read online at http://dceg.cancer.gov/radia/res35.html. ■

—Steven Simon, Ph.D.



Left, a diagram of side view of tank of water in which dose rates are measured during exposure to x-rays to simulate scattering characteristics of human tissue. Right, a mannequin of a six-year-old child (made of material with a composition similar to human tissue) with imbedded dosimeters to help determine radiation exposures in real patients. (Both figures, Stovall M, et al. *Radiation Res* 2006;166:141–157)

GAIL INAUGURATES BRESLOW LECTURES

Norman Breslow (left) and Bruce Weir (right) of the University of Washington presented Mitchell Gail (center) with the Breslow Distinguished Lectureship Award. *(Photograph Credit: Pete Mesling)*

In August, **Mitchell Gail, M.D., Ph.D.,** Chief of the Biostatistics Branch (BB), delivered the inaugural Norman E. Breslow Distinguished Lecture at the School of Public Health and Community Medicine of the University of Washington at Seattle. Dr. Gail's talk was entitled "Absolute risk: Clinical applications and controversies."

The lectureship was established this year by the Department of Biostatistics of the University of Washington to honor the scientific contributions of Norman Breslow, Professor and former Chairman of the Department. Dr. Breslow made pioneering contributions to the advancement of biostatistical methodology in survival analysis, generalized linear mixed models, and the design of case-control and cohort studies. The lectureship will be awarded each year to an individual who has made important scholarly contributions to the advancement of biostatistical methodology and its applications in the health sciences.

Dr. Gail received his M.D. from Harvard Medical School in 1968 and his Ph.D. in statistics from George Washington University in 1977. He joined NCI in 1969 and became Chief of BB in 1994. Dr. Gail has made major methodologic contributions in several areas, including characterizing the motility of cells in tissue culture, evaluating diagnostic tests and serial markers, designing and analyzing clinical trials and epidemiologic studies, AIDS research, and development of absolute risk models, such as the widely used "Gail model" to project breast cancer risk. ■

SPRING 2006 INTRAMURAL RESEARCH AWARD WINNERS

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

Competition was stiff this spring. The winners were **Parveen Bhatti, Ph.D.,** of the Radiation Epidemiology Branch, for his proposal, "Assessing DNA damage and telomere length in biologic samples collected before and after cancer diagnoses"; **Jill Koshiol, Ph.D.,** of the Genetic Epidemiology Branch, for "Evaluation of the presence and functionality of human papillomavirus in esophageal squamous cell carcinoma"; and **Sharon Savage, Ph.D.,** of the Clinical Genetics Branch, for her proposal entitled "Telomere biology and cancer risk."

Proposals were reviewed by members of the NCI Board of Scientific Counselors or other extramural scientists with appropriate expertise and by senior DCEG scientists. The proposals were judged on their potential for significant scientific and public health impact, innovation, interdisciplinary nature, ability to achieve the objectives within the proposed timeframe and resources, and relevance to the mission of the Division.

Intramural Research Award Winners: Sharon Savage, Parveen Bhatti, and Jill Koshiol.

TOOL HELPS CLINICIANS ESTIMATE MELANOMA RISK

Melanoma usually develops slowly and can often be cured when detected as a thin lesion in the outer layer of skin. Invasive melanoma can be deadly, however. A risk assessment tool was developed by **Thomas Fears, Ph.D.,** a senior investigator in the Biostatistics Branch, and **Margaret Tucker, M.D.,** Chief of the Genetic Epidemiology Branch and Director of the Human Genetics Program, to estimate the five-year absolute risk of melanoma and to efficiently identify individuals at increased risk of melanoma.

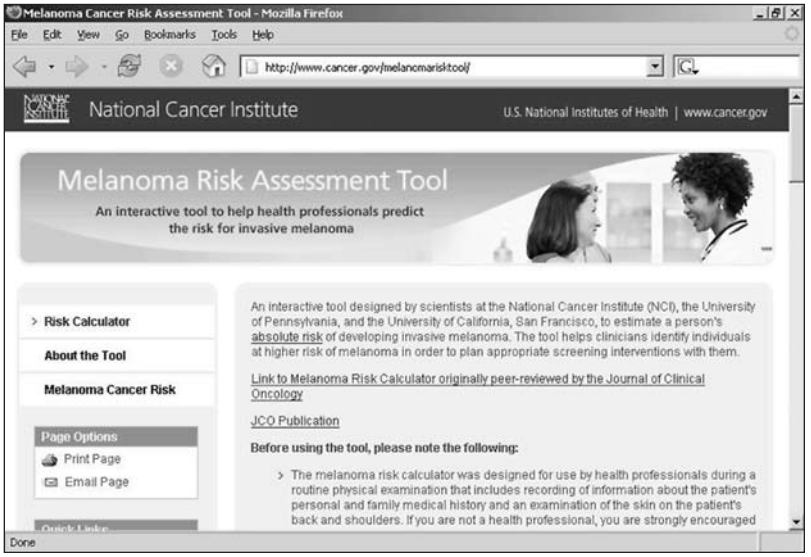
Routine screening of the general population for melanoma is not feasible due to the cost and high proportion of negative examinations. However, identifying patients at high risk and recommending interventions, including a complete skin examination, counseling to avoid sun exposures, regular self and professional surveillance, or participation in prevention trials, could promote detection of melanoma in its early stages when treatment is most effective.

The researchers developed relative risk models using data from a clinic-based case-control study of 718 non-Hispanic white patients with invasive cutaneous melanoma and 945 controls. An easy-to-use risk assessment tool was then derived for use by primary care providers by combining the relative risk models with incidence and mortality rates to produce absolute risk models. A practitioner asks two questions (for men, complexion and severe sunburn history, and for women, complexion and suntan ability) and examines only the back and shoulders. The back and shoulders were chosen as indicators of melanoma risk because those areas are easily evaluated for moles, freckling, and sun damage during routine physical examinations and because the number of nevi (benign moles, one of the most important determinants of risk) on the back is highly correlated with the total number of nevi on the whole body.

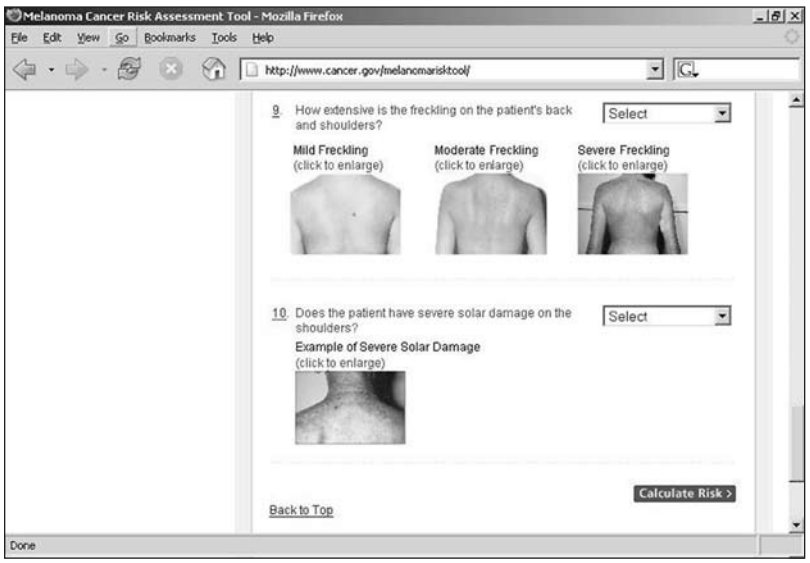
The questions and clinical observations characterize important risk factors for melanoma. These risk factors account for 86 percent of melanoma cases among men and 89 percent among women. The proportion of cases attributable to the factors in the model was stable across different ages and amounts of sun exposure. The observed *individual* absolute risks varied widely, depending on age, other host characteristics, and geographic area.

The tool is available at www.cancer.gov/melanomarisktool. ■

—Nicole M. Keesecker



The web site for the calculator includes supplementary guides to help clinicians explain melanoma risk to patients.



The online calculator is easy to use, and includes visual aids such as these photographs to help clinicians characterize a patient's degree of freckling.

SALLIE ROSEN KAPLAN FELLOWS JOIN DIVISION

Kim Danforth, Sc.D., and **Mahboobeh Safaeian, Ph.D.,** recently joined the Hormonal and Reproductive Epidemiology Branch (HREB) as the Division's newest Sallie Rosen Kaplan postdoctoral fellows.

The Sallie Rosen Kaplan Fellowship for Women Scientists in Cancer Research is an annual competition for postdoctoral fellows who wish to train in any of NCI's intramural research settings. Made possible by a bequest from Ms. Kaplan to the Foundation for NIH (FNIH), fellows receive a supplement to their first-year stipend. Because this year's applicants were exceptional, NCI and FNIH selected two fellows to train in DCEG.

Sallie Rosen Kaplan Fellows: Mahboobeh Safaeian and Kim Danforth.

Dr. Danforth comes to DCEG from the Harvard School of Public Health, where she earned a doctoral degree in epidemiology with minors in biostatistics and cancer prevention. Her dissertation focused on the relationship between hormones, reproductive and lifestyle factors, and ovarian cancer using data from the Nurses' Health Study. Prior to her training at Harvard, Dr. Danforth received an M.P.H. from the University of California, Berkeley, where she first experienced the multidisciplinary nature of epidemiology and public health. "I really enjoyed how the biology and medicine, statistics, behavioral science, and policy came together to comprehensively address public health concerns, and it is exciting to see this collaborative spirit here at NCI," Dr. Danforth said.

In HREB, Dr. Danforth will continue her work investigating the role of modifiable and lifestyle risk factors in the development of ovarian cancer with **James Lacey, Ph.D.,** whose research inspired her to apply to the fellowship program. She will also explore new avenues of research with **Ann Hsing, Ph.D.,** including the genetic epidemiology of prostate cancer and disparities in prostate cancer risk among various racial and ethnic groups.

Before receiving a Ph.D. in epidemiology at the Johns Hopkins Bloomberg School of Public Health, Dr. Safaeian earned an M.P.H. from the University of Pittsburgh and served as a senior programmer and analyst on the ALIVE (**A**IDS **L**ink to **I**ntra**v**enous **E**xperience) study, a 15-year prospective cohort study examining the natural history of HIV transmission among drug users in Baltimore. Building on her experience in infectious disease epidemiology, Dr. Safaeian focused her doctoral training on the natural history of human papillomavirus (HPV) infection in an HIV-endemic population in Rakai, Uganda, and wrote her thesis on the utility of self-collected vaginal specimens for studying the epidemiology of HPV infection.

"In this rural community (Rakai), there is a lack of services as well as a reluctance to go for a pelvic exam, so it was exciting to observe that low-cost screening done by the women at home performed as well as if the specimens were collected by a clinician," Dr. Safaeian said. She embraces the opportunity to broaden her research during her fellowship. "I am excited to be part of a team with such a comprehensive focus on prevention of cervical cancer, from the etiologic agent and its natural history to screening, diagnostics, and treatment for different stages of the lesions. Initially I will be involved in projects being conducted by the HPV research team in HREB: the evaluation of new diagnostic tools, clinical epidemiology to assess optimal screening and management strategies, and natural history studies, so that I may best determine which area of the field I will ultimately focus on."

Dr. Safaeian will be working under the mentorship of **Philip Castle, Ph.D., M.P.H.,** and **Mark Schiffman, M.D., M.P.H.,** both investigators in HREB. ■

—Alyssa Minutillo, M.P.H.

ALUMNI ILLUSTRATE VARIETY OF CAREER CHOICES

In June, three former DCEG scientists spoke to Division fellows about careers in epidemiology. To help the approximately 75 percent of fellows who leave DCEG for jobs elsewhere, **Shelia Hoar Zahm, Sc.D.,** Deputy Director of DCEG, invited several alumni to share their experiences. Three presenters described the many opportunities for epidemiologists and biostatisticians outside of DCEG, gave practical advice on how to find and negotiate for these jobs, and discussed further training. Dr. Jerome Wilson, Associate Director for Scientific Program Operations at the NIH National Center on Minority Health and Health Disparities; Dr. Sandra L. Melnick, Scientific Review Administrator at the NIH Center for Scientific Review; and Dr. Howard D. Strickler, Professor of Epidemiology and Population Health at the Comprehensive Cancer Center of Albert Einstein College of Medicine, shared their experiences before a standing room–only group of fellows and other staff.

Dr. Wilson spoke about his extensive experience in the pharmaceutical industry, most recently as Director/Team Leader for Global Outcomes Research at Pfizer, Inc. Dr. Wilson received a B.A. in chemistry and mathematics from Dillard University in New Orleans, an M.A. in immunology and biochemistry from Harvard Medical School, and a Ph.D. in epidemiology from the University of North Carolina at Chapel Hill. He was a fellow in DCEG's Radiation Epidemiology Branch from 1984 to 1986 and left for an academic position at Howard University. He later moved to the pharmaceutical industry, where he worked for several companies and was responsible for leading several drugs through U.S. Food and Drug Administration approval and for developing pharmacoeconomics and outcomes research strategies for products in several disease areas. Dr. Wilson described the types of research that epidemiologists are called upon to conduct in the pharmaceutical industry; the utility of training in budgeting, project management, and personnel management; tips for tailoring curricula vitae for specific jobs; and the importance of executive search firms and networking.

DCEG Alumni: Jerome Wilson, Howard Strickler, and Sandra Melnick.

Other divisions of NCI are common destinations for DCEG fellows. Dr. Melnick discussed the role of an extramural program director, a position she held in DCEG (when the Division briefly had an extramural component) and the Division of Cancer Control and Population Sciences (DCCPS). Dr. Melnick received her bachelor's, master's, and doctoral degrees from the University of Alabama at Birmingham; conducted postdoctoral research at the University of Washington; and was an Assistant Professor at the University of Minnesota before coming to NIH. At DCCPS, Dr. Melnick oversaw a broad epidemiology grants portfolio with emphasis on infectious agents in the etiology of malignancies and the epidemiology of non-Hodgkin lymphoma. In addition, she helped found the NCI Consortium of Cohorts and several of the international case-control consortia, such as InterLymph. In her presentation, she described how extramural program directors can help shape the future of their fields. With knowledge of ongoing research, they can anticipate future directions and take steps to make the necessary resources available. They identify gaps or underfunded areas and

provide crucial advice to investigators on how to write a successful grant. Her description of these interactions was also valuable for fellows considering careers as academic researchers. In addition, she described the activities and skills involved in her current position overseeing grant application reviews.

Dr. Strickler, a former fellow and Senior Clinical Investigator in DCEG's Viral Epidemiology Branch, received his bachelor's degree from Lehigh University in Pennsylvania and his medical degree from New York Medical College. After an internship at the University of Pittsburgh, he went to Johns Hopkins University, where he completed a residency in general preventive medicine, received an M.P.H., and was a postdoctoral research fellow. He now runs a successful academic research program at Albert Einstein School of Medicine focusing on HIV and human papillomavirus. In his presentation, he explained how to be successful and effective in academia. He provided advice on seeking out a supportive environment with people who are willing and able to collaborate scientifically, and who would mentor them in applying for grants. Academic jobs offer benefits such as the chance to work with scientists in other disciplines, the freedom to work on a wide range of topics, and the pleasure of working with and mentoring junior faculty and students. He recommended that young scientists request help from DCEG scientists when seeking work and continue to collaborate when possible. He encouraged fellows to learn as much as possible about field study management, budgeting, and building research teams.

Division alumni who work in different venues (such as academia, industry, regulatory agencies, nonprofit organizations, scientific writing, and health policy organizations) are valuable resources for fellows seeking information for their next position. ■

—Shelia Hoar Zahm, Sc.D.

MOLECULAR EPIDEMIOLOGISTS WIN NEW AWARDS

To increase research funding opportunities for fellows and tenure-track scientists and to promote molecular epidemiologic research, DCEG held a Molecular Epidemiology Research Funding Award competition earlier this year. As part of the 2006 Molecular Epidemiology Course, participants developed research proposals on topics related to the course agenda, such as methodologic studies assessing or improving methods for collecting, shipping, processing, and storing biospecimens; biorepository maintenance; state-of-the-art specimen analysis techniques; biomarker development; and pilot projects for etiologic studies.

Four proposals were selected to receive funding up to $10,000. The winners were **Jiyoung Ahn, Ph.D.,** a postdoctoral fellow in the Nutritional Epidemiology Branch, for her project entitled "Isolation and quantification of transmembrane receptors from frozen whole blood"; **Elizabeth Bluhm, M.D., M.P.H.,** a Cancer Prevention Fellow in the Radiation Epidemiology Branch, for her proposal entitled "Extraction of whole tumor genomes from archival tumor specimens"; **Mia Gaudet, Ph.D.,** a research fellow in the Hormonal and Reproductive Epidemiology Branch, for her project on "Optimizing tissue sampling and DNA extraction from formalin-fixed paraffin-embedded breast tumors to facilitate methylation assays in epidemiologic studies"; and **Sharon Savage, M.D.,** a tenure-track investigator in the Clinical Genetics Branch, for her proposal on "Comparative analysis of telomere lengths."

Course lecturers evaluated the proposals based on feasibility, originality, potential value, and relevance to DCEG research and applicability to multiple Division studies and cancer sites.

—Kristin Kiser, M.H.A.

Molecular Epidemiology Proposal Winners: (front) Mia Gaudet and Jiyoung Ahn; (back) Sharon Savage and Elizabeth Bluhm.

SUMMER FELLOWS ARE INTRODUCED TO EPIDEMIOLOGY

DCEG's summer fellowship program exposes bright and energetic students to the fields of epidemiology biostatistics and genetics. Such an experience can have a profound influence on the directions students pursue in school and later in their careers. Each year, DCEG receives about 250 applications for summer fellowships, from which 15 to 20 students are accepted. This year, 20 young people worked in DCEG, including two medical, two doctoral, and six M.P.H. students; eight undergraduates; and two high school students.

Summer fellows met with their mentors and Division leaders. *(Photograph Credit: Mindy Kaufman)*

DCEG summer mentors are dedicated to making the summer experience valuable. Last spring, **Jorge Toro, M.D.,** a tenure-track investigator in the Genetic Epidemiology Branch (GEB), was contacted by his alma mater, Cornell University, to mentor a biology major, **Michael Weinreich,** for the summer. Mr. Weinreich had a unique opportunity to work in an epidemiology laboratory. "It was a pleasure and an honor to mentor such a bright student," Dr. Toro said.

Twelve fellows presented their work at the Eighth Annual DCEG Summer Poster Session, organized by **Kristin Kiser, M.H.A.,** Fellowship Coordinator, and **Erin Toops** from the Office of Education (OE). The poster session was preceded by an awards ceremony and discussion with **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, **Shelia Hoar Zahm, Sc.D.,** DCEG Deputy Director, and **Demetrius Albanes, M.D.,** Chief of OE and a senior investigator in the Nutritional Epidemiology Branch (NEB). Both the students and their mentors agreed that the highlight of the event was hearing these senior scientists recount the various paths their careers took before coming to DCEG. Thirteen of the summer fellows also presented posters at the NIH Summer Poster Session the previous day.

Two of the summer fellows came to DCEG through the highly competitive NCI Introduction to Cancer Research Careers (ICRC) program. The ICRC awardees were **Travis Gayles,** a third-year medical student at the University of Illinois at Urbana-Champaign, and **Elizabeth Guzmán-Morales,** a recent biology graduate from the University of Puerto Rico. ICRC offers students from diverse and/or disadvantaged backgrounds an opportunity to work at NCI for a summer. The award covers summer housing and travel expenses. For further details, visit the ICRC web site, http://icrc.nci.nih.gov.

"… this is an important dimension of the Division's training portfolio, one that aims to inspire young students early in their careers and, it is hoped, to interest some of them in cancer epidemiology and public health."

The summer program also offered DCEG postdoctoral fellows an opportunity to gain mentoring experience. **Gabriel Chodick, Ph.D.,** a postdoctoral fellow in the Radiation Epidemiology Branch (REB), noted, "I was interested in mentoring a summer student because I've found that college students often ask the most clever and original questions. Unlike graduate students, they are free from professional conventions." From the student's perspective, there are valuable lessons to be learned about the real world of scientific research. Dr. Chodick's summer student, **Paul Waltz,** a rising senior in biology at Penn State University, observed that "before this experience, I always had the impression that if something was published, it was correct. However, I'll be sure to be more critical of any scientific literature I'm exposed to in the future." Dr. Chodick commented that "the highlight of Paul's summer experience was preparing a Letter to the Editor in which he raised several important questions regarding the validity of the conclusions of previous ecological studies on the protective effects of sunlight in preventing cancer."

Summer applicants can submit online applications starting in mid-November to the NIH Summer Application site (http://www.training.nih.gov/student/index.asp), indicating their interest in participating in epidemiology programs at NCI. To assist with the review process, the Division created a summer fellowship web page, (http://www.dceg.cancer.gov/summer.html), where students interested in DCEG may complete an online summary application.

Dr. Albanes aptly summarizes the DCEG Summer Program, stating that "this is an important dimension of the Division's training portfolio, one that aims to inspire young students early in their careers and, it is hoped, to interest some of them in cancer epidemiology and public health. I am always impressed with what the summer fellows accomplish with their mentors in such a short period." ■

Research Posters/Projects by the 2006 Summer Fellows

Longitudinal study of three multiple-case Waldenstrom's macroglobulinemia families. **Melissa Berg,** Pomona College. Mentor: **Mary Lou McMaster, M.D.** (GEB)

Prospective study of antioxidant nutrients and fruits and vegetables in relation to renal cell carcinoma: The ATBC Study. **Monica Bertoia,** Yale University School of Public Health. Mentors: **Demetrius Albanes, M.D.,** and **Margaret Wright, Ph.D.** (NEB)

Development of a data dictionary for the NIH-AARP Diet and Health Study. **Madeleine Blank,** University of Michigan. Mentor: **Traci Mouw, M.P.H.** (NEB)

Dietary intake of vitamin E and risk of upper gastrointestinal cancer in the AARP Study. **Sarah Carman,** University of Michigan. Mentors: **Sanford Dawsey, M.D.,** and **Farin Kamangar, M.D., Ph.D.** (NEB)

Use of a multiplex oligonucleotide ligation assay to test differences in the distribution of selected SNPs in an esophageal cancer case-control study. **Erica Dawsey,** University of Michigan. Mentors: **Nan Hu, M.D., M.P.H., David Ng, M.D.,** and **Philip Taylor, M.D., Sc.D.** (GEB)

Arsenic exposure assessment for Maine public water supplies in a case-control study of bladder cancer in New England. **John Oliver L. DeLancey,** Emory University Rollins School of Public Health. Mentor: **Laura Beane-Freeman, Ph.D.** (Occupational and Environmental Epidemiology Branch)

Study of serum high-density lipoprotein cholesterol and non-Hodgkin lymphoma risk in the ATBC cohort. **Travis Gayles,** University of Illinois at Urbana-Champaign. Mentors: Dr. Albanes and **Unhee Lim, Ph.D.** (NEB)

One-carbon metabolism and cancers of the colon and rectum: Literature review of prospective epidemiologic studies. **Elizabeth Guzmán-Morales,** University of Puerto Rico. Mentors: **Stephanie Weinstein, Ph.D.,** and **Rachael Stolzenberg-Solomon, Ph.D.** (NEB)

Early stages of a qualitative study of young women who are carriers of a BRCA 1 or 2 mutation and explored the impact of a BRCA mutation on young women's intentions and behaviors related to formation and maintenance of permanent couple relationships. **Lindsey Hoskins,** University of Maryland, Baltimore. Mentor: **June Peters, M.S., C.G.C.** (Clinical Genetics Branch [CGB])

Iodine deficiency in Chornobyl-affected areas of Ukraine and Belarus. **Miriam Ishak,** University of Michigan School of Public Health. Mentors: **Maureen Hatch, Ph.D.,** and **Alina Brenner, M.D., Ph.D.** (REB)

A review paper entitled *"Esophageal cancer in Northeastern Iran"* and an original paper entitled *"Ginseng and cancers of the stomach, esophagus, and head and neck in Shanghai Women's Health Study."* **Kourosh Kahkeshani,** Emory University. Mentor: Dr. Kamangar

Improving web access to the NIH-AARP Diet and Health Study. **Casey Kelsey,** St. Paul's High School. Mentor: Ms. Mouw

Immunoglobulin and lymphocyte subset studies in the inherited bone marrow failure syndromes cohort. **Sara Khaghani,** University of California, Los Angeles. Mentors: **Blanche Alter, M.D., M.P.H.,** and **Neelam Giri, M.D.** (CGB)

Associations between catechol-o-methyltransferase (COMT) polymorphisms and obesity, smoking, and alcohol. **Zhao Ellie Lan,** Churchill High School. Mentor: **Sophia Wang, Ph.D.** (Hormonal and Reproductive Epidemiology Branch)

Mammography shifts breast cancer population age-structure and tumor characteristics. **Anne Reiner,** Yale University School of Public Health. Mentors: **William Anderson, M.P.H., M.D., Rayna Matsuno, M.S.,** and **Ruth Pfeiffer, Ph.D.** (Biostatistics Branch)

Protocol design for a proposed field study in Kazakhstan. **Sara Schonfeld,** Johns Hopkins Bloomberg School of Public Health. Mentors: **Charles Land, Ph.D., Martha Linet, M.D., M.P.H., Kiyohiko Mabuchi, M.D., Dr.P.H.,** and **Steve Simon, Ph.D.** (REB)

The cancer screening practices of adult survivors of retinoblastoma. **Victoria Sheen,** University of California, San Diego. Mentor: **Ruth Kleinerman, M.P.H.** (REB)

Analysis of serum alpha-tocopherol and dietary tocopherols and pancreatic cancer in the ATBC cohort. **Seth E. Sheffler-Collins,** University of Michigan School of Public Health. Mentor: Dr. Stolzenberg-Solomon

Association between melanoma, colon, breast, ovary, NHL, and prostate cancer incidence rates and residential UV dose: A multi-country ecological study. **Paul Waltz,** Penn State University. Mentors: **Gabriel Chodick, Ph.D.,** and **D. Michal Freedman, Ph.D.** (REB)

Birt-Hogg-Dubé gene mutation detection in familial and sporadic kidney cancer. **Michael Weinreich,** Cornell University. Mentors: **Jorge Toro, M.D.,** and **Ousmane Toure, Ph.D.** (GEB), with Ms. Ming-Hui Wei (SAIC)

FELLOWS AWARDED DOCTORAL DEGREES

A critical element of DCEG's mission is training the next generation of scientists, including predoctoral students, in cancer epidemiology and related fields. In most cases, predoctoral candidates conduct their dissertation research using scientific resources at DCEG and are jointly mentored by DCEG scientists and faculty at their educational institution. This year, three DCEG predoctoral fellows finished their research and received doctoral degrees.

Sarah Daugherty, Parveen Bhatti, and Sonja Berndt.

Sonja Berndt, Pharm.D., Ph.D., a fellow in the Occupational and Environmental Epidemiology Branch (OEEB), successfully defended her thesis on "Genetic polymorphisms in DNA repair genes and the risk of colorectal neoplasia" and received her Ph.D. from the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health. Her mentors were **Richard Hayes, D.D.S., Ph.D.** (OEEB), and Dr. Kathy Helzlsouer of Johns Hopkins University.

Parveen Bhatti, Ph.D., a fellow in the Radiation Epidemiology Branch (REB), defended his doctoral thesis before faculty from the Environmental Health Program at the University of Washington School of Public Health. His dissertation was on DNA double-strand break repair polymorphisms, ionizing radiation exposure, and breast cancer risk. His mentors were **Alice Sigurdson, Ph.D.** (REB), Dr. Michael Yost, and Dr. Harvey Checkoway of the University of Washington.

This spring, **Sarah Daugherty, Ph.D.,** a fellow in OEEB, completed her doctoral thesis titled "Alpha-methylacyl CoA racemase: A candidate gene for prostate cancer and colorectal adenomas in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial." Her doctoral degree was from the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health, with a concentration in genetics and cancer epidemiology. Her primary mentors were Dr. Hayes, Dr. Elizabeth Platz, Dr. Yin Yao, and Dr. Dani Fallin of Johns Hopkins University.

Training support for Drs. Berndt and Bhatti came in part from the NIH Graduate Partnerships Program. Dr. Daugherty began her career at DCEG as a summer volunteer in the Genetic Epidemiology Branch under the mentorship of **Lynn Goldin, Ph.D.,** and **Ruth Pfeiffer, Ph.D.,** Biostatistics Branch. ■

Honghong Zhu

FELLOW WINS BEST POSTER AWARD

At the third NIH Graduate Research Symposium held in May, **Honghong Zhu, M.D.,** a fellow in the Occupational and Environmental Epidemiology Branch, received one of three Best Poster awards for her poster, "Secondhand smoke and breast cancer risk in the Shanghai Women's Health Study." Judging criteria were clarity, organization, and the potential impact of the research. Dr. Zhu's topic was also selected by the organizing committee as "an outstanding example of research on which to give an oral presentation." Dr. Zhu is a doctoral student in the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health.

ANNUAL FELLOWS' TOWN HALL MEETING

In June, the DCEG Committee of Scientists (COS) sponsored the sixth annual DCEG Fellows' Town Hall Meeting. Pre- and postdoctoral fellows met with senior Division leaders to discuss the training program. Fellows were invited to raise issues about anything that affected the quality of their training experience or career development at DCEG. The meeting was coordinated by COS Fellow Representatives **Christine Mueller, D.O.,** Clinical Genetics Branch, **Kimberly Kerstann, Ph.D.,** Genetic Epidemiology Branch (GEB), and **Lindsay Morton, Ph.D.,** Hormonal and Reproductive Epidemiology Branch.

Kimberly Kerstann and Christine Mueller, along with Lindsay Morton (not shown), co-organized this year's DCEG Fellows' Town Hall Meeting.

Fellows heard from the NIH Fellows' Committee (FELCOM) Representatives, **Honghong Zhu, M.D.,** Occupational and Environmental Epidemiology Branch (OEEB), and **Shih-Chen Chang, Ph.D.,** Nutritional Epidemiology Branch (NEB). Drs. Zhu and Chang described activities of FELCOM and its subcommittees and their role in enhancing the intramural training program and fostering communication among fellows and the NIH community. The representatives urged DCEG fellows to participate in FELCOM.

Aaron Blair, Ph.D. (OEEB), Chair of COS, provided an overview of the role of COS and discussed issues raised by fellows in the 2006 DCEG Annual Survey. **Shelia Hoar Zahm, Sc.D.,** Deputy Division Director, presented statistics on the DCEG fellowship program, including the average length of stay, areas of future employment, and the importance of fellows' contributions to DCEG publications. **Demetrius Albanes, M.D.** (NEB), Chief of the Office of Education (OE), discussed the essential role of mentoring within DCEG and outlined plans for upcoming OE-sponsored workshops addressing critical elements of training and mentoring. **Margaret Tucker, M.D.,** Chief of GEB and Director of the Human Genetics Program, spoke about the importance of mentoring and project development for fellows at DCEG.

Following the presentations, the meeting shifted to a roundtable format, pairing two or more speakers—including **Robert Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, and **Kristin Kiser, M.H.A.** (OE)—with smaller groups of fellows for informal discussions. Participants were encouraged to raise topics of concern, offer candid feedback regarding their fellowship experience, and share ideas for improving the training program. COS is reviewing the issues raised and will work with the fellows and Division leadership to enhance the DCEG fellowship experience. ■

—Christine Mueller, D.O., and
Kimberly Kerstann, Ph.D.

BRANCH RESCUES RESOURCES ON RADIOACTIVE FALLOUT

Dosimetry, or the assessment of radiation doses and risks from exposure to radioactive fallout from worldwide nuclear testing, is a longstanding area of active research by the Radiation Epidemiology Branch (REB). Health physicists **Steven Simon, Ph.D.,** and **André Bouville, Ph.D.,** lead these efforts.

Steven Simon is shown with about half of the collection. *(Photograph Credit: Harold Beck)*

Laboratory reports and other "gray literature" (documentary material that is not commercially published) produced between the 1950s and the 1980s are difficult to find but are an important source of information when deriving historical measurements of environmental radioactivity. Recently, Dr. Simon was able to rescue a large collection of historical documents about fallout and related subjects from the Department of Homeland Security's Environmental Measurements Laboratory in New York City, which was closing and discarding its records. The collection is now being sorted and scanned into electronic form by REB staff. After the information is converted, the physical documents will be donated to the Nevada Atomic Testing History Institute, located at the University of Nevada.

SCIENTIFIC HIGHLIGHTS

BILIARY TRACT CANCER

Klatskin Tumor

Hilar cholangiocarcinomas, or Klatskin tumors, are anatomically defined as extrahepatic cholangiocarcinomas; however, in the second edition of the ICD-O (ICD-O-2), these tumors were assigned a histology code, 8162/3, Klatskin, which was cross-referenced to intrahepatic cholangiocarcinoma. To assess the impact of this misclassification on site-specific incidence rates, the investigators examined the classification of hilar cholangiocarcinomas within nine registries in the U.S. population with data from the Surveillance, Epidemiology, and End Results (SEER) Program and calculated the annual percent changes (APC) in site-specific cholangiocarcinoma incidence during 1992–2000. The authors show that 91 percent (246 of 269) of hilar cholangiocarcinomas were misclassified using the code 8162/3, Klatskin, resulting in an overestimation of intrahepatic cholangiocarcinoma incidence by 13 percent and underestimation of extrahepatic cholangiocarcinoma incidence by 15 percent. However, even after the exclusion of tumors that were coded to the histology code 8162/3, Klatskin, age-adjusted annual intrahepatic cholangiocarcinoma incidence increased during this period (APC = 4%, CI = 2%–6%, $p < 0.001$). **(Welzel TM, McGlynn KA, Hsing AW, O'Brien TR, Pfeiffer RM. Impact of classification of hilar cholangiocarcinomas (Klatskin tumors) on the incidence of intra- and extrahepatic cholangiocarcinoma in the United States. *J Natl Cancer Inst* 2006;98:873–875)**

BLADDER CANCER

Smoking and Bladder Cancer

The effects of dose, type of tobacco, cessation, inhalation, and environmental tobacco smoke exposure on bladder cancer risk were examined among 1,219 patients with newly diagnosed bladder cancer and 1,271 controls recruited from 18 hospitals in Spain. Current smokers (men: odds ratio [OR] = 7.4, CI = 5.3–10.4; women: OR = 5.1, CI = 1.6–16.4) and former smokers (men: OR = 3.8, CI = 2.8–5.3; women: OR = 1.8, CI = 0.5–7.2) had significantly increased risks of bladder cancer compared with nonsmokers, with significant trends for increasing duration and amount smoked. After adjustment for duration, risk was 40 percent higher in smokers of black tobacco than that in smokers of blond tobacco (OR = 1.4; CI = 0.98–2.0). Compared with risk in current smokers, a significant inverse trend in risk with increasing time since quitting smoking blond tobacco was observed (≥ 20 years cessation: OR = 0.2, CI = 0.1–0.9). No trend in risk with cessation of smoking black tobacco was apparent. Compared with men who inhaled into the mouth, risk increased for men who inhaled into the throat (OR = 1.7; CI = 1.1–2.6) and chest (OR = 1.5; CI = 1.1–2.1). Cumulative occupational exposure to environmental tobacco smoke seemed to confer increased risk among female nonsmokers but not among male nonsmokers. After eliminating the effect of cigarette smoking on bladder cancer risk in the study population, the male-to-female incidence ratio decreased from 8.2 to 1.7, suggesting that much of male excess of bladder cancer is explained by cigarette smoking rather than exposures to other bladder carcinogens. **(Samanic C, Kogevinas M, Dosemeci M, Malats N, Real FX, Garcia-Closas M, Serra C, Carrato A, Garcia-Closas R, Sala M, Lloreta J, Tardon A, Rothman N, Silverman DT. Smoking and bladder cancer in Spain: Effects of tobacco type, timing, environmental tobacco smoke, and gender. *Cancer Epidemiol Biomarkers Prev* 2006;15:1348–1354)**

BREAST CANCER

Predicting Breast Cancer Risk

To improve the discriminatory power of the Gail model to predict absolute risk of invasive breast cancer, the authors previously developed a relative risk model that incorporated mammographic density from data on white women in the Breast Cancer Detection Demonstration Project (BCDDP). The relative risk model included data on the distribution of age at birth of first live child, affected mother and/or number of affected sisters, number of previous benign breast biopsy examinations, and weight from the 2000 National Health Interview Survey. The authors combined the model with data on the conditional distribution of density given other risk factors in BCDDP, with breast cancer incidence rates from the SEER Program, and with national mortality rates, then compared the absolute five-year risk projections from the new model with those from the Gail model on 1,744 white women. The relative risk model predicted higher risks than the Gail model for women with a high percentage of dense breast area. However, the average risk projections from the new model in various age groups were similar to those from the Gail model, suggesting that the new model is well calibrated. This new model incorporating mammographic density promises modest improvements in discriminatory power compared with the Gail model but needs to be validated with independent data. **(Chen J, Pee D, Ayyagari R, Graubard B, Schairer C, Byrne C, Benichou J, Gail MH. Projecting absolute invasive breast cancer risk in white women with a model that includes mammographic density. *J Natl Cancer Inst* 2006;98:1215–1226)**

Prenatal Diethylstilbestrol Exposure

Whether prenatal diethylstilbestrol (DES) exposure is associated with risk of breast cancer was assessed in a cohort of DES-exposed and unexposed women followed since the 1970s (see Figure 1). During follow-up, 102 incident cases of invasive breast cancer occurred, with 76 cases among DES-exposed women (98,591 person-years) and 26 among unexposed women (35,046 person-years). The overall age-adjusted incidence rate ratio (IRR) was 1.40 (CI = 0.89–2.22). For breast cancer occurring at age 40 years and older, the IRR was 1.91 (CI = 1.09–3.33) and for cancers occurring at age 50 years and older, it was 3.00 (CI = 1.01–8.98). **(Palmer JR, Wise LA, Hatch EE, Troisi R, Titus-Ernstoff L, Strohsnitter W, Kaufman R, Herbst AL, Noller KL, Hyer M, Hoover RN. Prenatal diethylstilbestrol exposure and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2006;15:1509–1514)**

GASTROINTESTINAL CANCER

Reducing Precancerous Gastric Lesion Prevalence

A randomized trial was conducted to test the effects of one-time *Helicobacter pylori* treatment and long-term vitamin or garlic supplements in reducing the prevalence of advanced precancerous gastric lesions among residents of Shandong Province, China, who had undergone baseline endoscopies in 1994. In 1995, 3,365 eligible subjects were randomly assigned in a factorial design to three interventions or placebos: amoxicillin and omeprazole for two weeks in 1995 (*H. pylori* treatment); vitamin C, vitamin E, and selenium for 7.3 years (vitamin supplement); and aged garlic extract and steam-distilled garlic oil for 7.3 years (garlic supplement). Subjects underwent endoscopies with biopsies in 1999 and 2003, and the prevalence of precancerous gastric lesions was determined by histopathologic examination of seven standard biopsy sites. *H. pylori* treatment resulted in statistically significant decreases in the combined prevalence of severe chronic atrophic gastritis, intestinal metaplasia, dysplasia, or gastric cancer in 1999 (OR = 0.77; CI = 0.62–0.95) and in 2003 (OR = 0.60; CI = 0.47–0.75), and it had favorable effects on the average histopathologic severity and on progression and regression of precancerous gastric lesions in 2003. *H. pylori* treatment did not reduce the combined prevalence of dysplasia or gastric cancer. However, fewer subjects receiving *H. pylori* treatment (19/1,130; 1.7%) than receiving placebos (27/1,128; 2.4%) developed gastric cancer (adjusted $p = 0.14$). No significant favorable effects were seen for garlic or vitamin supplements. **(You WC, Brown LM, Zhang L, Li JY, Jin ML, Chang YS, Ma JL, Pan KF, Liu WD, Hu Y, Crystal-Mansour S, Pee D, Blot WJ, Fraumeni JF Jr, Xu GW, Gail MH. Randomized double-blind factorial trial of three treatments to reduce the prevalence of precancerous gastric lesions. *J Natl Cancer Inst* 2006;98:974–983)**

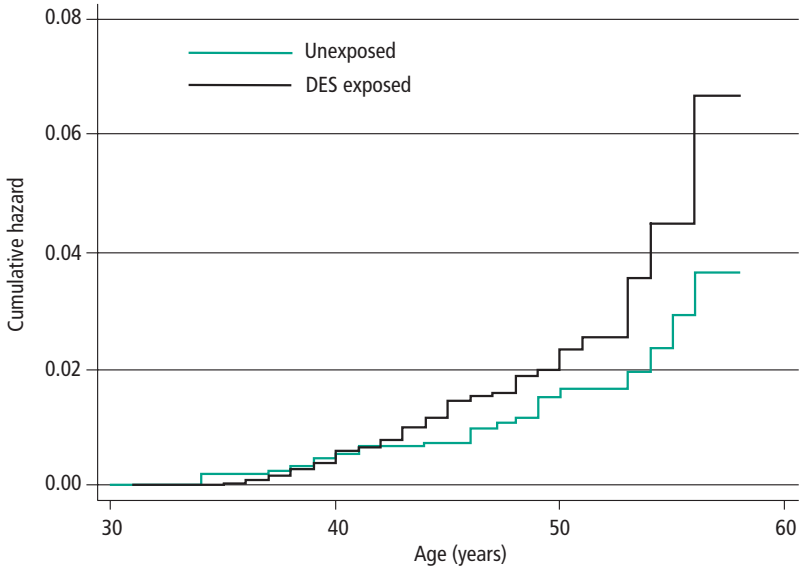


Figure 1. Cumulative hazard plots for prenatal DES exposure in relation to risk of breast cancer. (Palmer JR, et al. 2006)

Inflammation-related Genes

The association of colorectal adenoma with 19 single nucleotide polymorphisms (SNPs) in a range of proinflammatory *(IL1B, IL6, IL8, TNF,* and *LTA)* and anti-inflammatory *(IL4, IL10,* and *IL13)* cytokines and other inflammation-related genes *(PTGS2* and *PPARG)* was investigated in a study of 244 cases of colorectal adenoma and 231 polyp-free controls. Compared with being homozygous for the common allele, heterozygosity at the *IL1B*-31 (C > T) locus was associated with an OR for colorectal adenoma of 1.8 (CI = 1.2–2.9). Homozygous carriers of the *IL8*-251-A allele were at 2.7-fold increased risk of adenoma (CI = 1.5–4.9) compared with homozygosity for the common T allele, whereas carriage of at least one *IL8*-251-A allele conferred 1.5-fold increased odds of disease (CI = 1.0–2.4). Among those who did not use nonsteroidal anti-inflammatory drugs (NSAIDs), there was an association between the *IL10*-819-T/T genotype and adenoma compared with the common *IL10*-819-C/C genotype (OR = 3.9; CI = 1.1–13.6), which was not evident among NSAID users (OR = 0.7; CI = 0.3–1.5; p for interaction = 0.01). **(Gunter MJ, Canzian F, Landi S, Chanock SJ, Sinha R, Rothman N. Inflammation-related gene polymorphisms and colorectal adenoma. *Cancer Epidemiol Biomarkers Prev* 2006;15:1126–1131)**

KAPOSI SARCOMA

Kaposi Sarcoma and Gene Variants

Using genomic DNA extracted from 133 classic Kaposi sarcoma (CKS) cases and 172 Kaposi sarcoma-associated herpesvirus (KSHV)–latent nuclear antigen-positive, population-based controls in Italy without HIV infection, the risk of CKS associated with 28 common genetic variants in 14 immune-modulating genes was examined. Haplotypes were estimated for *IL1A, IL1B, IL4, IL8, IL8RB, IL10, IL12A, IL13,* and *TNF.* Compared with controls, CKS risk was decreased with 1235T/-1010G-containing diplotypes of *IL8RB* (OR = 0.49; CI = 0.30–0.78), whereas risk was increased with diplotypes of *IL13* containing the promoter region variant 98A (rs20541, alias +130; OR = 1.88; CI = 1.15–3.08) when considered in multivariate analysis. Data provide preliminary evidence that variants in immune-modulating genes could influence the risk of CKS. **(Brown EE, Fallin D, Ruczinski I, Hutchinson A, Staats B, Vitale F, Lauria C, Serraino D, Rezza G, Mbisa G, Whitby D, Messina A, Goedert JJ, Chanock SJ. Associations of classic Kaposi sarcoma with common variants in genes that modulate host immunity. *Cancer Epidemiol Biomarkers Prev* 2006;15:926–934)**

LYMPHOMA

Autoimmunity and Hodgkin Lymphoma

To assess the risk of Hodgkin lymphoma associated with autoimmune conditions, population-based linked registry data from Sweden and Denmark were used. Thirty-two separate autoimmune and related conditions were identified from hospital diagnoses in 7,476 subjects with Hodgkin lymphoma, 18,573 matched control subjects, and more than 86,000 first-degree relatives of cases and controls. The authors found increased risks of Hodgkin lymphoma associated with personal histories of rheumatoid arthritis (OR = 2.7; CI = 1.9–4.0); systemic lupus erythematosus (OR = 5.8; CI = 2.2–15.1), sarcoidosis (OR = 14.1; CI = 5.4–36.8), and immune thrombocytopenic purpura (OR = infinity, p = 0.002). An increase in Hodgkin lymphoma risk was associated with family histories of sarcoidosis (OR = 1.8; CI = 1.01–3.1) and ulcerative colitis (OR = 1.6; CI = 1.02–2.6). **(Landgren O, Engels EA, Pfeiffer RM, Gridley G, Mellemkjaer L, Olsen JH, Kerstann KF, Wheeler W, Hemminki K, Linet MS, Goldin LR. Autoimmunity and susceptibility to Hodgkin lymphoma: A population-based case-control study in Scandinavia. *J Natl Cancer Inst* 2006;98:1321–1330)**

Cyclin D1 Splice Variant

To investigate the role of cell cycle gene variations in lymphomagenesis, associations in polymorphisms from seven candidate genes in 1,172 non-Hodgkin lymphoma (NHL) cases and 982 population-based controls were evaluated. The cyclin D1 (*CCND1*) splice variant G870A (rs603965) increased NHL risk (OR_{AA} = 1.4; CI = 1.1–1.8, p for trend = 0.021), which was consistent for four B-cell subtypes. As CCND1 expression indicates poor NHL prognosis, these results, if confirmed, would support its potentially dual importance in NHL etiology and survival. **(Wang SS, Cozen W, Severson RK, Hartge P, Cerhan JR, Davis S, Welch R, Rothman N, Chanock SJ. Cyclin D1 splice variant and risk for non-Hodgkin lymphoma. *Hum Genet* 2006;120:297–300)**

DNA Repair Genes

The authors examined 34 variants in 19 genes within or related to five DNA repair pathways among 1,172 cases and 982 matched controls in a population-based NHL study in Los Angeles, Seattle, Detroit, and the state of Iowa from 1998–2000. Cases were more likely than controls to have the *RAG1* 820 Arg/Arg (OR = 2.7; CI = 1.4–5.0) than Lys/Lys genotypes, with evidence of a gene dosage effect (p for trend = 0.0008), and less likely to have the *LIG4* (DNA Ligase IV) 9 Ile/Ile (OR = 0.5; CI = 0.3–0.9) than Thr/Thr genotype (p for trend = 0.03) in the non-homologous end joining (NHEJ)/V(D)J pathway. These NHEJ/V(D)J-related gene variants represent promising candidates for further studies of NHL etiology. **(Hill DA, Wang SS, Cerhan JR, Davis S, Cozen W, Severson RK, Hartge P, Wacholder S, Yeager M, Chanock SJ, Rothman N. Risk of non-Hodgkin lymphoma (NHL) in relation to germline variation in DNA repair and related genes. *Blood* 2006; July 20 [E-pub ahead of print])**

Ocular Non-Hodgkin Lymphoma

A recent report suggesting that ocular adnexal NHL may be related to *Chlamydia psittaci* infection underscores the need for reliable epidemiologic data for this malignancy. Population-based incidence data from the SEER Program were examined. During 1992–2001, ocular (i.e., eye and adnexa) NHL rates per 100,000 person-years for both sexes were highest among Asians/Pacific Islanders, lower in whites, and lower still in blacks. Incidence increased with advancing age and showed little difference by sex, in contrast to other NHLs, which occurred predominantly in males. During 1975–2001, there was a rapid and steady increase in incidence of ocular NHL, with annual increases of 6.2 percent and 6.5 percent among white males and females, respectively, and with no evidence of peaking (see Figure 2). By contrast, other NHLs showed evidence of peaking in recent years. **(Moslehi R, Devesa SS, Schairer C, Fraumeni JF Jr. Rapidly increasing incidence of ocular non-Hodgkin lymphoma. *J Natl Cancer Inst* 2006;98:936–939)**

MALIGNANT MELANOMA

MC1R Gene

Germline variants in *MC1R,* the gene encoding the melanocortin-1 receptor, and sun exposure increase risk for melanoma in whites. The majority of melanomas that occur on skin with little evidence of chronic sun-induced

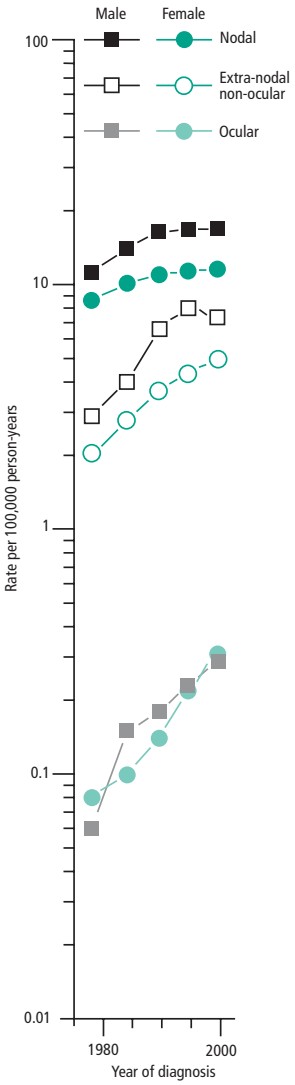


Figure 2. Age-adjusted non-Hodgkin lymphoma incidence trends among whites by site and sex. (Moslehi R, et al. 2006)

damage (non-CSD) have mutations in the *BRAF* oncogene, whereas in melanomas on skin with marked CSD, these mutations are less frequent. In two independent white populations, the authors show that *MC1R* variants are strongly associated with *BRAF* mutations in non-CSD melanomas. In this tumor subtype, the risk for melanoma associated with *MC1R* is due to an increased risk of developing melanomas with *BRAF* mutations. **(Landi MT, Bauer J, Pfeiffer RM, Elder DE, Hulley B, Minghetti P, Calista D, Kanetsky PA, Pinkel D, Bastian BC. MC1R germline variants confer risk for *BRAF*-mutant melanoma. *Science* 2006;313:521–522)**

METHODS

Mendelian Mutation Prediction Models

People with familial histories of disease often consult genetic counselors about their chances of carrying mutations that increase disease risk. Commonly encountered errors in reported family history can significantly distort predictions and thus can alter the clinical management of people undergoing counseling, screening, or genetic testing. The author derived general results about the distortion in the carrier probability estimate caused by misreported diagnoses in relatives and showed that the Bayes factor, which channels all family history information, has a convenient and intuitive interpretation. The author focused on the ratio of the carrier odds given correct diagnosis versus given misreported diagnosis to measure the impact of errors. Misreported age of diagnosis usually caused less distortion than misreported diagnosis. **(Katki HA. Effect of misreported family history on Mendelian mutation prediction models. *Biometrics* 2006;62:478–487)**

Haplotype-based Association Analysis

Genetic epidemiologic studies often collect genotype data at multiple loci within a genomic region of interest from a sample of unrelated individuals. One method for analyzing such data is to assess whether haplotypes are associated with the disease phenotype. For many study subjects, however, the exact haplotype configuration on the pair of homologous chromosomes cannot be derived with certainty from the available locus-specific genotype data. The authors considered estimating haplotype-specific association parameters in the Cox proportional hazards model, using genotype, environmental exposure, and the disease endpoint data collected from cohort or nested case-control studies. Alternative expectation-maximization algorithms for estimating haplotype frequencies from cohort and nested case-control studies were studied. Based on a hazard function of the disease derived from the observed genotype data, a semiparametric method for joint estimation of relative risk parameters and the cumulative baseline hazard function is proposed. The method is greatly simplified under a rare disease assumption, for which an asymptotic variance estimator is also proposed. **(Chen J, Chatterjee N. Haplotype-based association analysis in cohort and nested case-control studies. *Biometrics* 2006;62:28–35)**

Multiple Hypothesis Testing

In case-control studies of unrelated subjects, gene-based hypothesis tests consider whether SNPs, haplotypes, or both are associated with disease. Standard statistical tests are available that control the false-positive rate at the nominal level over all polymorphisms considered. More powerful tests can be constructed that use permutation resampling to account for correlations between polymorphisms and test statistics. A key question is whether the gain in power is large enough to justify the computational burden. The authors compared the computationally simple Simes Global Test to the min P test, which considers the permutation distribution of the minimum p-value from marginal tests of each SNP. In simulation studies incorporating empirical haplotype structures in 15 genes, the min P test controlled type I error and was modestly more powerful than the Simes test, by 2.1 percent on average. When disease susceptibility was conferred by a haplotype, the min P test sometimes—but not always—under-performed the haplotype analysis. A resampling-based omnibus test combining the min P and haplotype frequency test controlled type I error and closely tracked the more powerful of the two component tests. This test achieved consistent gains in power (5.7% on average) compared to a simple Bonferroni test of Simes and

haplotype analysis. **(Chen BE, Sakoda LC, Hsing AW, Rosenberg PS. Resampling-based multiple hypothesis testing procedures for genetic case-control association studies. *Genet Epidemiol* 2006;30:495–507)**

NUTRITION

Aspartame-Containing Beverages

Some laboratory studies have suggested that consumption of the artificial sweetener aspartame could be associated with the risk of hematopoietic cancers and gliomas. This hypothesis was investigated among 285,079 men and 188,905 women aged 50 to 71 in the NIH-AARP Diet and Health Study. Aspartame intake was derived from a baseline self-administered questionnaire that queried consumption of aspartame-containing beverages (soda, fruit drinks, sweetened iced tea, and aspartame added to hot coffee and tea) during the past year. During more than five years of follow-up, 1,888 hematopoietic cancers and 315 malignant gliomas were ascertained from eight state cancer registries. Higher levels of aspartame intake were not associated with the risk of overall hematopoietic cancer (risk ratio [RR] for ≥ 600 mg/day = 0.98; CI = 0.76–1.27), glioma (RR for ≥ 400 mg/day = 0.73; CI = 0.46–1.15; *p* for inverse linear trend = 0.05) or histologic subtypes. **(Lim U, Subar AF, Mouw T, Hartge P, Morton LM, Stolzenberg-Solomon R, Campbell D, Hollenbeck AR, Schatzkin A. Consumption of aspartame-containing beverages and incidence of hematopoietic and brain malignancies. *Cancer Epidemiol Biomarkers Prev* 2006;15:1654–1659)**

Overweight, Obesity, and Mortality

Body mass index (BMI) in relation to the risk of death from any cause was studied among 527,265 U.S. men and women, aged 50 to 71 years at enrollment in 1995–1996 in the NIH-AARP cohort. BMI was calculated from self-reported weight and height. During a maximum follow-up of 10 years, 61,317 participants (42,173 men and 19,144 women) died. Initial analyses showed an increased risk of death for the highest and lowest categories of BMI among both men and women, in all racial or ethnic groups, and at all ages. When the analysis was restricted to people who had never smoked, an elevated risk of death was associated with upper levels of overweight and with obesity among men and women (see Figure 3). In analyses of BMI during midlife (age 50 years) among those who had never smoked, the risk of death increased by 5 to 49 percent among overweight persons and by two to more than three times among obese persons, while the risk of death among underweight persons was attenuated. **(Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R, Hollenbeck A, Leitzmann MF. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med* 2006;355:763–778)**

Obesity and Site-specific Cancer Risks

The link between obesity and cancer and the effect of change in BMI over six years was studied among 362,552 Swedish men who underwent at least one physical examination from 1971 to 1992 and who were followed until death or the end of 1999. Incident cancer cases were identified by linkage to the Swedish cancer registry. Compared to men of normal weight, obese men had a slightly increased risk of all cancers combined (RR = 1.1; CI = 1.0–1.2). The risks were most pronounced for esophageal adenocarcinoma (RR = 2.7; CI = 1.3–5.6); renal cell carcinoma (RR = 1.8; CI = 1.4–2.4); malignant melanoma (RR = 1.4; CI = 1.1–1.7); and cancers of the colon (RR = 1.7; CI = 1.5–2.0), rectum (RR = 1.4; CI = 1.1–1.7), and liver (RR = 3.6; CI = 2.6–5.0). Risk of esophageal squamous cell carcinoma was elevated for underweight men whose BMI was less than 18.5 (RR = 3.1;

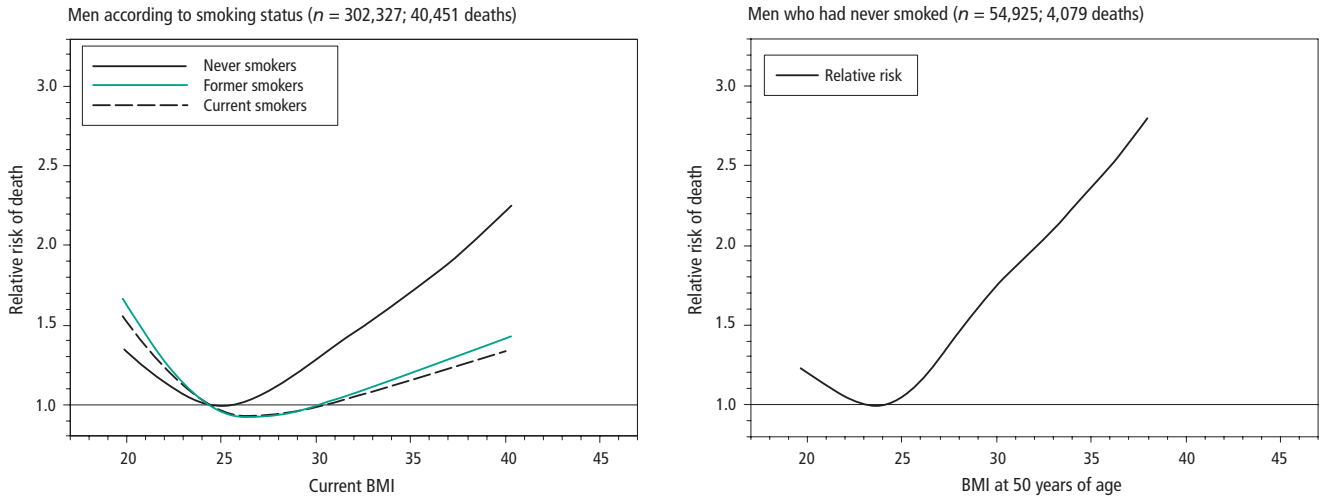


Figure 3. Multivariate relative risks of death in relation to BMI among men. Left panel shows analyses stratified by smoking status, and right panel shows relative risks in relation to BMI at age 50. (Adams KF, et al. 2006)

CI = 1.1–8.3). An excess risk for cancers of the pancreas and connective tissue was observed only among nonsmokers. Compared to men whose weight remained stable, men with more than a 15 percent increase in BMI after six years of follow-up had an elevated risk of pancreatic and renal cell cancers. **(Samanic C, Chow WH, Gridley G, Jarvholm B, Fraumeni JF Jr. Relation of body mass index to cancer risk in 362,552 Swedish men. *Cancer Causes Control* 2006;17:901–909)**

THYROID CANCER

Thyroid Cancer after Chornobyl

Between 1998 and 2000, a cohort of 13,127 individuals younger than 18 years of age who were residents of areas in Ukraine heavily contaminated by radioactive iodine isotopes, particularly (131)I, at the time of the Chornobyl accident in 1986 was screened for any thyroid pathology by ultrasound and palpation. Forty-five pathologically confirmed cases of thyroid cancer were found. Thyroid cancer showed a strong, monotonic, and approximately linear relationship with individual thyroid dose estimate ($p < 0.001$), yielding an estimated excess relative risk of 5.25 per gray (CI = 1.70–27.5). Greater age at exposure was associated with decreased risk of radiation-related thyroid cancer, although this interaction effect was not statistically significant. In the absence of Chornobyl radiation, 11.2 thyroid cancer cases would have been expected compared with the 45 observed, a reduction of 75 percent (CI = 50%–93%). **(Tronko MD, Howe GR, Bogdanova TI, Bouville AC, Epstein OV, Brill AB, Likhtarev IA, Fink DJ, Markov VV, Greenebaum E, Olijnyk VA, Masnyk IJ, Shpak VM, McConnell RJ, Tereshchenko VP, Robbins J, Zvinchuk OV, Zablotska LB, Hatch M, Luckyanov NK, Ron E, Thomas TL, Voilleque PG, Beebe GW. A cohort study of thyroid cancer and other thyroid diseases after the Chornobyl accident: Thyroid cancer in Ukraine detected during first screening. *J Natl Cancer Inst* 2006;98:897–903)**

DCEG PEOPLE IN THE NEWS

Kenneth Moritsugu, Acting Surgeon General, USPHS, presented Linda Morris Brown with the Exemplary Service Medal.

Between April and August, **Blanche Alter, M.D., M.P.H.,** Clinical Genetics Branch (CGB), spoke about her research on inherited bone marrow failure syndromes at the New York Society for the Study of Blood meeting, Pediatric Hematology and Oncology Conference at Weill Medical College of Cornell University, Children's Hospital Oakland Research Institute, and Camp Sunshine in Casco, Maine.

In September, **Robert Biggar, M.D.,** Viral Epidemiology Branch (VEB), gave a talk entitled "Hodgkin lymphoma and immunity: Insights into pathogenesis from the HIV/AIDS experience" at the Staten Serum Institut, Copenhagen, where he has been assigned to work for one year.

In September, **CAPT Linda Morris Brown, Dr.P.H.,** Biostatistics Branch (BB), was honored for her four-year tenure as the Health Services Chief Professional Officer at a succession ceremony held at the Uniformed Services University of the Health Sciences in Bethesda.

Kenneth Cantor, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB), recently chaired the Working Group of the 94th International Agency for Research on Cancer Monograph in Lyon, France, which evaluated the carcinogenicity of ingested nitrate, nitrite, and cyanobacterial peptide toxins. **Mary Ward, Ph.D.** (OEEB), chaired the working group's Epidemiology Subcommittee. A brief summary of the evaluation was published in *Lancet Oncology* in August.

In July, **Neil Caporaso, M.D.,** Genetic Epidemiology Branch (GEB), chaired

NEW FELCOM REPS

Anil Chaturvedi, Ph.D., Viral Epidemiology Branch, and **Jocelyn Weiss, Ph.D., M.P.H.,** Occupational and Environmental Epidemiology Branch (OEEB), have been appointed to represent DCEG on the NIH Fellows Committee, also known as FELCOM. They are replacing **Shih-Chen Chang, Ph.D.,** Nutritional Epidemiology Branch, and **Honghong Zhu, M.D.** (OEEB).

a symposium on "Genetics of tobacco use: Hope and hype" at the 13th World Conference on Tobacco or Health. He reviewed recent findings on how heredity influences smoking and other key exposures involved in cancer, and he highlighted new directions in the field, such as the integration of genetic studies of behavior into large population-based investigations.

In July, **Philip Castle, Ph.D., M.P.H.,** Hormonal and Reproductive Epidemiology Branch (HREB), spoke on "Epidemiology and prevention of human papillomavirus-related cancers" to students in the summer NIH Undergraduate Scholarship Program, which identifies and nurtures young scientists from disadvantaged backgrounds.

Nilanjan Chatterjee, Ph.D. (BB), delivered invited talks on "Analysis of case-control studies in genetic epidemiology" at an International Biometric Society meeting in Flagstaff, Arizona in May and the North American Congress of Epidemiology in Seattle in June. In August, he gave an invited presentation entitled "Analysis of two-phase studies of gene-environment interaction" at the Joint Statistical Meeting in Seattle.


Amanda Cross

Amanda Cross, Ph.D., Nutritional Epidemiology Branch (NEB), has been appointed tenure-track investigator in NEB. Dr. Cross has a Ph.D. in nutrition and cancer from the University of Cambridge. She joined NEB as a postdoctoral fellow in 2003 and has focused her research on meat and meat-mutagens as risk factors for a variety of cancers, including colorectal, prostate, and pancreatic cancers. Dr. Cross is also the principal investigator of the CONCeRN study, a colonoscopy screening study among asymptomatic women.

In July, **Eric Engels, M.D., M.P.H.** (VEB), gave a talk entitled "The transplant cancer match study" at a meeting of the Technical Advisory Committee to the Scientific Registry of Transplant Recipients in Chicago.


Neal Freedman

In August, **Neal Freedman, Ph.D., M.P.H.** (NEB), won the Best Poster Award at the Yrjö Jahnsson Foundation Medical Symposium on Etiology and Prevention of Digestive Tract Cancers, held in Porvoo, Finland. His poster was entitled "Evaluating acetaldehyde as a potential carcinogen for esophageal cancer in Linxian, China."

Neelam Giri, M.D. (CGB), presented "National Cancer Institute's Diamond-Blackfan Anemia Cohort: A preliminary report" at the Annual International Diamond-Blackfan Anemia Consensus Conference in New York in March.

In September, **James Goedert, M.D.** (Chief of VEB), spoke on "Challenges in providing medical care in a developing nation—A focus on Haiti" at the U.S. Food and Drug Administration Clinical Reviewers Education Program. In October, Dr. Goedert spoke about "Infection and disease determinants: Kaposi Sarcoma in Sicily" at the 30th Congress of the Italian Epidemiology Association in Palermo.

At the Annual Melanoma Genetics Consortium Meeting in Geneva in June, **Alisa Goldstein, Ph.D.** (GEB), gave a presentation on "*MC1R* and multiple primary melanomas."

In July, **Barry Graubard, Ph.D.** (BB), gave an invited short course entitled "Analysis of health surveys: Sample survey methods for biostatisticians" at the 23rd International Biometric Conference in Montreal. In August, Dr. Graubard chaired the General Methodology Program for the 2006 Joint Statistical Meetings in Seattle. Dr. Graubard and **Mitchell Gail, M.D., Ph.D.** (Chief of BB), along with the CDC authors, received a Charles C. Shepard Science Award from CDC for their paper "Excess deaths associated with underweight, overweight, and obesity" published in *JAMA* in 2005.

Mark Greene, M.D. (Chief of CGB), spoke on "Genes associated with cancer" at the National Human Genome Research Institute's Genetic Counselor Seminar Series in April, "Risk reducing interventions: Update on GOG 199" at the Lynn Cohen Foundation Ovarian Cancer Symposium in New York in May, and "Epidemiology of ovarian cancer" at the NCI Division of Cancer Prevention's (DCP) Summer Course in July.

Maureen Hatch, Ph.D. (Head of the Chornobyl Research Unit, Radiation Epidemiology Branch [REB]), has been appointed vice-chair of the NCI Special Studies Institutional Review Board.

In June, **Allan Hildesheim, Ph.D.** (HREB), **Mark Schiffman, M.D., M.P.H.** (HREB), and **Diane Solomon, M.D.** (DCP and Adjunct Investigator, HREB), along with Dr. Douglas Lowy and Dr. John Schiller (both in the NCI Center for Cancer Research) received the DHHS Secretary's Award for Distinguished Service in recognition of their work on the human papillomavirus vaccine.

In late May, **Jose Jeronimo, M.D.** (HREB), gave a lecture on "Challenges for the diagnosis and treatment of cervical cancer in low-resource settings" at the 33rd Annual International Conference on Global Health in Washington, DC.

At the Annual Melanoma Genetics Consortium Meeting in Geneva in June,

Maria Teresa Landi, M.D., Ph.D. (GEB), gave a talk on "*BRAF* mutations and melanoma subtypes." Later that month at the 28th International Congress in Occupational Health in Milan, Dr. Landi cochaired the session on "Application of molecular epidemiology in occupational and environmental health." At the same meeting, Dr. Landi also gave a presentation on "Gene-environment interaction in tumor causation: The example of cutaneous melanoma."

In May, **Mary Lou McMaster, M.D.** (GEB), gave an invited talk on "Understanding Waldenstrom's macroglobulinemia—The power of families" at a meeting of the Washington, DC chapter of the International Waldenstrom's Macroglobulinemia Foundation.

In May, **Ruth Pfeiffer, Ph.D.** (BB), delivered a talk titled "Discovery and validation of clinical markers from proteomics data for early detection of ovarian cancer: Some epidemiologic and statistical considerations" at the Biostatistics Seminar at the University of Innsbruck in Austria. In July, she spoke on "A colorectal cancer risk assessment tool" at the Workshop on Imaging Science Development for Cancer Prevention and Preemption in Gaithersburg, Maryland.

In August, **Charles Rabkin, M.D.** (VEB), spent two weeks as a temporary duty internist with the Indian Health Service (IHS). He was stationed in the Outpatient Clinic of Fort Yates IHS Hospital, the main facility serving the Standing Rock Sioux Reservation, on the North/South Dakota border.


Preetha Rajaraman

Preetha Rajaraman, Ph.D., has been promoted to research fellow. She began at REB as a predoctoral fellow in 2001 while working towards her Ph.D. in epidemiology at the Johns Hopkins Bloomberg School of Public Health. After graduation, Dr. Rajaraman accepted a postdoctoral fellowship in REB, where she continued her work on lead and brain tumors and also collaborated on studies of radiation exposure among U.S. radiological technologists, late effects of childhood irradiation, and health effects of medical irradiation.

Arthur Schatzkin, M.D., Dr.P.H. (Chief of NEB), gave two invited talks this summer: "Can biomarkers help us to understand the nutritional and lifestyle factors important in cancer prognosis?" at the AICR International Research Conference on Food, Nutrition, and Cancer in Washington, DC and "Biomarkers of dietary intake: A dream in nutritional epidemiology?" at the Etiology and Prevention of Digestive Tract Cancers meeting in Finland.

In June, **Steven Simon, Ph.D.** (REB), presented "Development of organ-specific external dose coefficients for dose reconstruction for medical personnel" at the 51st Annual Meeting of the Health Physics Society in Providence.

Philip Taylor, M.D., Sc.D. (GEB), presented "SNP arrays in cancer—An integrated approach" at the 97th AACR Meeting in Washington, DC in April. In the same month, Dr. Taylor spoke at the Lombardi Comprehensive Cancer Center at Georgetown University on "Selenium in the prevention of esophageal cancer." In July at the eighth International Symposium on Selenium in Biology and Medicine in Madison, Dr. Taylor presented a talk on "Selenium and cancer prevention: A community-based fortification plan in Linxian, China."

Jim Vaught, Ph.D., Office of the Director, has been appointed to the editorial board of *Cell Preservation Technology* and serves as senior editor for biorepository and biospecimen science for *Cancer Epidemiology, Biomarkers and Prevention*.

In July, **Margaret Wright, Ph.D.** (NEB), gave an invited talk on "Beta-carotene, smoking, and lung cancer" at the International Research Conference on Food, Nutrition, and Cancer in Washington, DC. Dr. Wright and **Demetrius Albanes, M.D.** (NEB and Chief of the Office of Education), received funding from the NIH Office of Dietary Supplements for their project entitled "How does vitamin E supplementation protect against clinically relevant prostate cancer in smokers?"

RADIATION DOSIMETRY CONFERENCE

In July, several staff in the Radiation Epidemiology Branch participated at BiodosEPR-2006, the Second International Conference on Biodosimetry and Seventh International Symposium on EPR Dosimetry and Applications held at the Uniformed Services University of the Health Sciences in Bethesda. **Kiyohiko Mabuchi, M.D., Dr.P.H.,** gave a plenary lecture on "Radiation dose and epidemiological risk estimation in atomic bomb survivors"; **Steven Simon, Ph.D.,** delivered the "Chairman's introduction to the consensus committee on retrospective dosimetry"; **André Bouville, Ph.D.,** gave the summary report from the Consensus Committee; and **Parveen Bhatti, Ph.D.,** spoke on an "International study of chromosome translocations in control populations."

COMINGS . . . GOINGS


Lesley Anderson

Lesley Anderson, Ph.D., has joined the Viral Epidemiology Branch (VEB) as an NCI Division of Cancer Prevention (DCP) Fellow. Dr. Anderson obtained her Ph.D. in epidemiology from Queen's University in Belfast. Her research focus has been on risk factors of esophageal carcinoma and Barrett's esophagus. She will be working primarily with **Eric Engels, M.D., M.P.H.** (VEB), and **James Goedert, M.D.** (Chief of VEB), on risk factors for non-Hodgkin lymphoma and classic Kaposi sarcoma.

Berit Bakke, Ph.D., M.S., a postdoctoral fellow in the Occupational and Environmental Epidemiology Branch (OEEB) for the past two years, has returned to Oslo, Norway. She worked with mentors **Patricia Stewart, Ph.D.,** and **Roel Vermeulen, Ph.D.,** on assessing trichloroethylene exposures in U.S. industry and evaluating immunological responses to pesticide exposures among farmers. In Norway, Dr. Bakke will resume her responsibilities as a senior engineer at the National Institute of Occupational Health.


Lisa Chu

Lisa Chu, Ph.D., M.P.H., has joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a DCP Fellow. In 2001, she received her Ph.D. in human and molecular genetics from the University of Texas M.D. Anderson Cancer Center. During 2002–2005, she was a postdoctoral fellow at Lawrence Berkeley National Laboratory. In 2006, she completed her M.P.H. in epidemiology under the mentorship of Dr. Gladys Block at the University of California, Berkeley. During her fellowship in HREB, she will work with **Ann Hsing, Ph.D.,** on the genetic, hormonal, and nutritional determinants of prostate cancer.


Gretchen Gierach

Gretchen Gierach, Ph.D., M.P.H., has joined HREB as a DCP Fellow. She completed her M.P.H. and Ph.D. degrees in epidemiology from the University of Pittsburgh. During her time in Pittsburgh, she worked on an ovarian cancer study with Dr. Roberta Ness and a study to identify hormonal determinants of mammographic densities with Dr. Francesmary Modugno. While in HREB, she will continue her research on mammographic densities and pursue risk factors for ovarian and endometrial cancers.

Meg Girstenblith, M.D., has left the Genetic Epidemiology Branch (GEB) to begin her dermatology residency at Johns Hopkins Hospital. During her stay in GEB, she worked with **Maria Teresa Landi, M.D., Ph.D.,** and **Alisa Goldstein, Ph.D.,** on a comprehensive evaluation of allele frequency of *MC1R* variants across populations.


Harry Haverkos

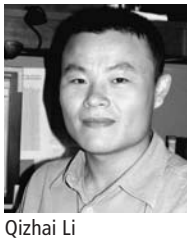
Harry Haverkos, M.D., has joined VEB as a Special Volunteer. Dr. Haverkos recently retired from the U.S. Public Health Service Commissioned Corps following a career with the CDC, National Institute on Drug Abuse, and U.S. Food and Drug Administration. During his time with VEB, he will focus on how environmental agents interact with infections to cause cancer.


Dean Hosgood

H. Dean Hosgood, III, M.P.H., has joined OEEB and will be working with **Qing Lan, M.D., Ph.D., M.P.H.,** on indoor air pollution, genetic susceptibility, and lung cancer, as well as with **Nathaniel Rothman, M.D., M.P.H., M.H.S.,** on the Shanghai Women's Health Study. He is a doctoral candidate in epidemiology at Yale University.

Daehee Kang, M.D., Ph.D., returned to Korea after a two-year sabbatical in OEEB. He worked on several projects, including the Agricultural Health Study, the Shanghai Women's Health Study, and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, and helped plan future collaborative initiatives in Asia.

Nicole Keesecker, M.A., a Health Communications Fellow working with **Betsy Duane-Potocki** in the Office of the Director (OD), completed her training program at NCI and returned to her hometown of Chicago. She plans to continue her public health career working in the non-profit arena.


Qizhai Li

Qizhai (James) Li, Ph.D., has joined the Biostatistics Branch (BB) as a postdoctoral fellow. In 2006, he received a Ph.D. in statistics from the Chinese Academy of Sciences, where his dissertation focused on population size estimation and its application in genomics. During his fellowship in BB, he will work with **Kai Yu, Ph.D.** (BB), on statistical genetics.


Dunstana Rabelo de Melo

Dunstana Rabelo de Melo, Ph.D., has joined the Radiation Epidemiology Branch (REB) as an Oak Ridge Institute for Science Education Senior Fellow. Dr. Melo has a Ph.D. in biophysics from the Federal University of Rio de Janeiro. She has training and experience in internal dosimetry, measurement techniques, and management of radiation accidents, including work on the Goiania radiation accident. Dr. Melo will work on several projects related to radiological terrorism and radiation dose estimation.

Roxana Moslehi, Ph.D., a postdoctoral fellow in GEB and BB, has left the Division to join the State University of New York at Albany School of Public Health as an Assistant Professor in Genetic Epidemiology, with an adjunct appointment in the Cancer Genomics Center. While in BB, Dr. Moslehi worked with mentors **Catherine Schairer, Ph.D.,** and **Mitchell Gail, M.D., Ph.D.,** on a variety of projects including the effect of *XP* gene dosage on reproduction and fetal/neonatal development, an analysis of ocular non-Hodgkin lymphoma, and a study of the effects of garlic supplements on cholesterol levels in the Shandong Intervention Trial. She also taught a number of courses at George Washington University in partnership with Dr. Paul Levine.


Karen Pitt

Karen Pitt, Ph.D., has joined DCEG's OD as Special Assistant for Biological Resources. Dr. Pitt received her doctoral degree in molecular biology from the University of California, Los Angeles. Dr. Pitt comes to NCI from her position as Director of Repository Services at BioReliance Invitrogen BioServices in Rockville. She was also Editor-in-Chief of the publication *Best Practices for Repositories I,* sponsored by the International Society for Biological and Environmental Repositories.

Joshua Rapkin, B.S., a predoctoral fellow with GEB, has been accepted into the University of Minnesota's Department of Biostatistics master's program. During his time in GEB, Mr. Rapkin worked with **Ola Landgren, M.D., Ph.D.,** looking at the relationship between respiratory tract infections and chronic lymphocytic leukemia.

Lori Sakoda, M.P.H., who served as a research analyst in HREB since 2001, has left DCEG to enroll in a Ph.D. program in epidemiology at the University of Washington in Seattle. In HREB, Ms. Sakoda contributed extensively to studies of various malignancies, including biliary tract, breast, liver, ovarian, prostate, testicular, and uterine cancers.

Sara Schonfeld, M.P.H., a predoctoral fellow in REB, recently completed a second summer fellowship and began her doctoral studies in epidemiology at the Johns Hopkins Bloomberg School of Public Health. Ms. Schonfeld was involved in the Branch's study of thyroid disease prevalence and fallout-associated radiation dose among childhood residents of villages near the Semipalatinsk Test Site in Kazakhstan. Last summer in Kazakhstan, she and her mentor **Nick Luckyanov, Ph.D.** (REB), helped improve dose reconstruction data on consumption and sources of milk during the period of nuclear bomb testing. This summer, Ms. Schonfeld was a key player in the Branch's planning efforts to use advanced survey methods to improve the database for this study.

Laveta Stewart, M.P.H. (GEB), has been accepted into the London School of Hygiene and Tropical Medicine master's program in immunology of infectious diseases. While in GEB, she worked with **Jorge Toro, M.D.,** and **Gladys Glenn, M.D., Ph.D.,** on the Hereditary Leiomyomatosis and Renal Cell Cancer Study.

PATRICIA STEWART RETIRES


Patricia Stewart

After a distinguished career in industrial hygiene and historical assessment of occupational exposures, **Patricia Stewart, Ph.D.,** has retired from OEEB. She pioneered many new procedures for developing quantitative estimates of historical exposures for both cohort and case-control studies. Dr. Stewart worked as an industrial hygienist at the state and federal level for eight years before joining NCI in 1982. She coupled this experience in monitoring exposures in the workplace with a new and creative approach to improve procedures for reconstructing exposures in epidemiologic studies. Not only did she develop new techniques, but she also had an impact on the development of computer systems to aid others in applying the new procedures for completing assessments.

Her international reputation as one of the premier industrial hygienists in the field comes not only from her scientific contributions, but also from her generosity of spirit. Dr. Stewart collaborated with investigators from institutions in many countries and mentored a new generation of researchers. She continues these activities even in retirement. Dr. Stewart is currently lecturing and teaching methods of exposure assessment at the Nofer Institute for Occupational Medicine in Lodz, Poland.

VISITING SCHOLAR ALICE WHITTEMORE

Dr. Alice Whittemore came to DCEG in May as the Division's latest Visiting Scholar. A mathematician by training, Dr. Whittemore has long been a pivotal leader in the field of cancer epidemiology through her efforts to develop rigorous statistical methods for complex linkage and genotype analyses in large epidemiologic and family studies.

Dr. Whittemore earned her B.S. from Marymount Manhattan College and her M.A. and Ph.D. from the City University of New York. After a decade devoted to "pure" mathematics, she redirected her work to applied mathematics and statistics. In 1974, she received a prestigious award from the Sloan Foundation and the Society of Industrial and Applied Mathematics and turned her mathematical background to examining environmental risk factors for cancer with Dr. Bernard Altshuler at New York University. Since that time, she has initiated several large studies on familial aggregation of breast, ovarian, and prostate cancers and designed novel methods of analyzing epidemiologic and genotyping data to uncover the role of gene-gene and gene-environment interactions in cancer risk.

In 1978, she joined Stanford University; she is now Director of the Epidemiology Program at the Stanford Comprehensive Cancer Center, overseeing a broad program of research in cancer etiology, surveillance, patterns of care, and cancer progression and survival.

In her seminar, entitled "The genetic epidemiology of breast and ovarian cancer," Dr. Whittemore discussed recent projects with the Breast Cancer Family Registry and the Family Registry for Ovarian Cancer, two NCI-funded multicenter initiatives designed to investigate the complex genetic and environmental etiologies of familial breast and ovarian cancers. Because *BRCA1* and *BRCA2* mutations are rare among the general population, clinic- and population-based cancer family registries provide valuable epidemiologic data and biologic resources to study the prevalence of mutations, cancer risk by ethnicity and racial group, and modifiers of genetic risk.

Margaret Tucker (left) presented Alice Whittemore with the DCEG Visiting Scholar Award. *(Photograph Credit: Geoffrey Tobias)*

Dr. Whittemore presented several analyses of registry data and discussed future avenues of research into heritable cancers associated with rare genetic variants. She emphasized the need to carefully evaluate preventive approaches in high-risk populations and to consider the clinical relevance of new genes detected through genome association studies. "I predict there will need to be a pooling of genome-wide data to gain power to detect uncommon mutations," she stated.

Following her talk, seminar co-hosts **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program (EBP), and **Margaret Tucker, M.D.,** Director of the Human Genetics Program and Chief of the Genetic Epidemiology Branch (GEB), honored Dr. Whittemore with a plaque commemorating her contributions to epidemiology and public health.

During the remainder of her visit, Dr. Whittemore met individually and in small groups with Division scientists. During a lunch with the Division's postdoctoral fellows moderated by **Regina Zeigler, Ph.D., M.P.H.** (EBP), she shared professional wisdom and offered career advice. In a discussion moderated by **Alisa Goldstein, Ph.D.** (GEB), Dr. Whittemore discussed the challenges encountered in family-based studies of cancer. **Stephen Chanock, M.D.,** Director of the NCI Core Genotyping Facility, moderated a session on genotyping, which was followed by a roundtable on common polymorphisms moderated by **Montserrat Garcia-Closas, M.D., Dr.P.H.,** Hormonal and Reproductive Epidemiology Branch. ■

—Alyssa Minutillo, M.P.H.

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