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Linkage

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IN THIS ISSUE:

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DCEG Holds Annual Retreat

The DCEG Senior Advisory Group (SAG) held its annual retreat in July at Rockwood Manor in Potomac, Maryland. For the first time, young investigators joined the senior faculty retreat to discuss future research directions that will prove critical to the continued success of the Division and the next generation of DCEG investigators.

Joseph F. Fraumeni, Jr., M.D., Director of DCEG, provided a Director's challenge by distinguishing between short-term and long-term planning and emphasizing the capacity of the intramural research program to take a long-range view and make gambles on high-risk, high-impact projects that are difficult to carry out in the extramural community. He emphasized the importance of framing scientific opportunities in the form of major questions to be answered and the development of strategies, technologies, and methodologies that will enable the Division to expedite the discovery and translation process.

Robert N. Hoover, M.D., Sc.D., Director of the Epidemiology and Biostatistics Program (EBP), described the value of long-term cohort studies and proposed a forward-thinking approach when considering future investigations: "Rather

Division retreat participants

DCEG *Linkage*

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than simply responding to isolated investigator-initiated concepts as they come forth or continuing to roll over our current investments, we must seek advice and input in developing priorities, and have a thoughtful examination of our entire portfolio of current and proposed research initiatives."

Patricia Hartge, Sc.D., Deputy Director of EBP and retreat program chair, then led a series of panel discussions that looked at design considerations, demographic patterns of cancer, and a variety of lifestyle, environmental, and genetic determinants that require further study. In breakout sessions, the participants identified themes and ways to prioritize tomorrow's research opportunities and stressed the importance of a cost-efficient leveraging of existing NCI and NIH resources. The day concluded with a wide-ranging question-and-answer session led by Dr. Fraumeni, Dr. Hoover, and **Margaret A. Tucker, M.D.,** Director of the Human Genetics Program and Chief of the Genetic Epidemiology Branch.

For the first time, young investigators joined the senior faculty retreat to discuss future research directions that will prove critical to the continued success of the Division and the next generation of DCEG investigators.

The retreat identified a number of areas of interest that will continue to be pursued, especially through ad hoc planning groups in a wide variety of areas. These include environmental and nutritional exposure assessment, genome-wide association studies, hormonal assay development, biorepository enhancements, development of a high-throughput molecular pathology core laboratory, the role of inflammation and immunity in causal mechanisms, and tumors that are rising in incidence (e.g., thyroid cancer). Some discussions centered around value-added enhancements to existing DCEG cohorts and potential options for planning the development of a future cohort that might be needed, for example, in collaboration with health maintenance organizations, the NCI Cancer Research Network, or a partly closed health service group, such as the U.S. military or the Department of Veterans Affairs.

The 2008 SAG Retreat marks the beginning of a multistep strategic planning process that will continue to unfold over the coming year. Both tenure-track and recently tenured investigators will actively participate along with senior members of the Division to explore and anticipate the most promising avenues for DCEG research in the 21st century. ■

—Catherine B. McClave, M.S.

DCEG WELCOMES VISITING SCHOLAR PAUL PHAROAH

In June, DCEG was honored to welcome Dr. Paul D.P. Pharoah for a two-day visit as a Visiting Scholar. Dr. Pharoah, a Cancer Research UK Senior Clinical Research Fellow in the Department of Oncology and the Strangeways Research Laboratory at the University of Cambridge, was hosted by **Montserrat García-Closas, M.D., Dr.P.H.,** Hormonal and Reproductive Epidemiology Branch (HREB).

Dr. Pharoah began his career practicing general medicine. After spending a year in Malawi working on a vaccine to prevent leprosy, Dr. Pharoah decided to specialize in public health. Upon his return to the United Kingdom, he earned a Diploma in Public Health and accepted a research fellowship with the Cancer Research Campaign (now known as Cancer Research UK) Human Cancer Genetics Group, where he became involved in a study of familial breast cancer under the mentorship of Sir Bruce Ponder. It was here that Dr. Pharoah received the comprehensive, cross-disciplinary training in epidemiology, molecular genetics, and laboratory techniques that made him uniquely poised to pursue the independent research program in genetic epidemiology that has earned him worldwide recognition. His current research portfolio includes studies of common genetic variation and breast and ovarian cancer susceptibility, polygenic models of cancer susceptibility (i.e., gene-gene interaction), and the role of germline genotype in determining the clinico-pathological characteristics of breast and ovarian cancer.

The highlight of Dr. Pharoah's visit was his seminar, titled "Common low-penetrance breast cancer susceptibility alleles: The clinical implications." Dr. Pharoah showed that novel breast cancer genetic susceptibility loci might prove useful. "We need to change the way we think about prevention," he urged. Genetic information could improve the ability to identify population subgroups at low and high risk in screening programs, which is more economical than the current practice of screening entire populations based on less predictive risk factors. In contrast, Dr. Pharoah demonstrated that using common susceptibility loci for individualized disease prevention is likely to be limited.

Following the seminar, **Joseph F. Fraumeni, Jr., M.D.,** Division Director, presented Dr. Pharoah with the DCEG Visiting Scholar Award in recognition of his leadership and vision in cancer genetics and epidemiology.

Dr. Pharoah's first roundtable discussion, moderated by **Mark E. Sherman, M.D.** (HREB), was dedicated to the etiologic heterogeneity of breast and ovarian cancer. **William F. Anderson, M.D., M.P.H.,** Biostatistics Branch (BB), presented data from his recent work, which describes the epidemiologic patterns for histologic subtypes of breast cancer. **Rose Yang, Ph.D., M.P.H.,** Genetic Epidemiology Branch, discussed her work on coexpression patterns of hormone markers and the identification of novel molecular subtypes of breast cancer. Dr. Pharoah then offered his perspective on which risk factors should be examined and what additional studies are still necessary. He emphasized that "even if a subtype classification is not prognostic, that does not mean that it is not biologically relevant."

Montserrat García-Closas, Paul Pharoah, and Joseph Fraumeni.

DCEG fellows had an opportunity to talk with Dr. Pharoah during a special luncheon session. He shared his experience as a graduate student and how he found his way to the field of cancer genetics and epidemiology. He encouraged young investigators to "be on the crest of the wave" of new technology by becoming "involved with new studies as the process of cutting-edge technologies to support them is under way."

In a second roundtable discussion, moderated by **Sholom Wacholder, Ph.D.** (BB), Dr. Pharoah commented on the value of common susceptibility loci in risk prediction, screening, and prevention. He stated, "the key to the risk-benefit decision is to consider absolute risk for the individual" rather than relative risk. He again emphasized that even if the clinical relevance of epidemiologic research results may not be immediately discernable, "the biological impact should not be overlooked."

Dr. Pharoah spent the remainder of his two-day visit in one-on-one sessions with other DCEG investigators discussing topics of mutual interest. ■

—Michael Donovan, Ph.D., and Alyssa Voss, M.P.H.

CHRISTIAN ABNET: SEEKING TO UNDERSTAND CANCER RISK

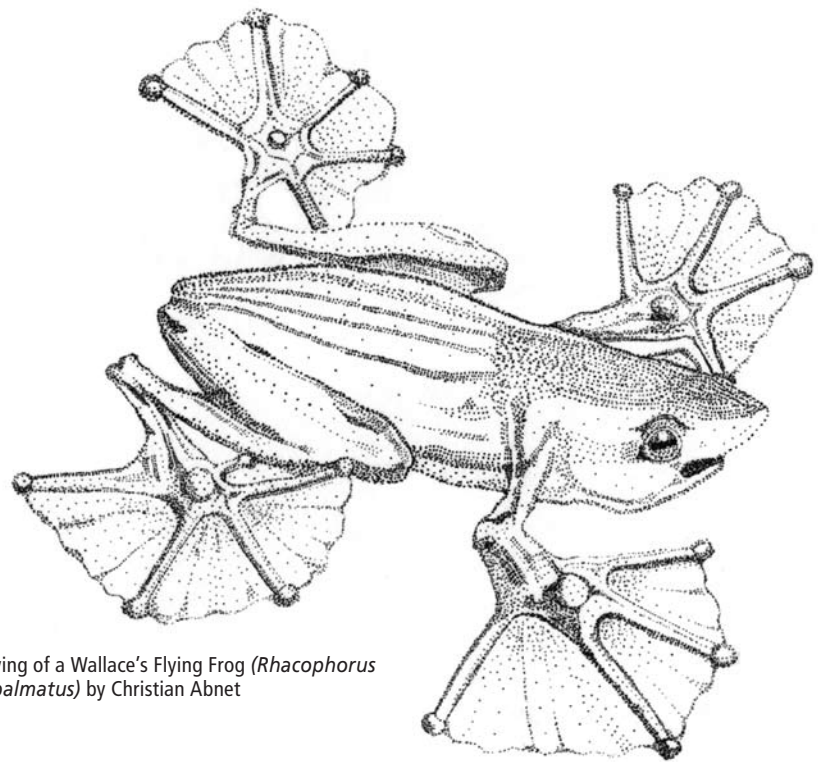
"Essentially, I couldn't decide what I wanted to do," recalled **Christian C. Abnet, Ph.D., M.P.H.,** Nutritional Epidemiology Branch (NEB), as he discussed his colorful background as an owl caller in Oregon for the U.S. Forest Service. "This work, censusing Northern Spotted Owls on Mt. Hood, allowed me time to think about a direction for my graduate education."

Deciding to pursue his interest in freshwater pollution, Dr. Abnet went on to complete his Ph.D. in environmental toxicology at the University of Wisconsin–Madison. After graduation, Dr. Abnet saw an advertisement in *Science* for the NCI Cancer Prevention Fellowship Program and thought it would be an interesting opportunity to move away from laboratory work. Because he had no epidemiology experience, he spent his first year completing an M.P.H. at the University of Minnesota in Minneapolis. For the second year of the fellowship, he came to the Center for Cancer Research in the Cancer Prevention Studies Branch, where he later took a position as staff scientist. He joined NEB with his appointment as a tenure-track investigator in 2005.

Thanks to the enduring relationships he formed during his fellowship, Dr. Abnet continues to collaborate with mentors **Sanford M. Dawsey, M.D.** (NEB), and **Philip R. Taylor, M.D., Sc.D.,** Genetic Epidemiology Branch. Working with Dr. Dawsey, **Farin Kamangar, M.D., Ph.D.** (NEB), and Iranian colleagues, Dr. Abnet recently completed accrual of a case-control study of esophageal squamous cell carcinoma (ESCC) in a high-risk population of northeastern Iran. Dr. Abnet's first analysis in the study found a strong association between tooth loss and increased risk of ESCC. This finding is similar to that of Dr. Abnet's previous prospective study of a high-risk rural population in China. Both studies show this association even in the absence of the two main etiologic factors for this disease in industrialized countries, alcohol and tobacco use. As Dr. Abnet explained, "the idea of tooth loss being related to cancer is not new, but relatively few epidemiological studies have looked at it, and there were no good data." This finding is important, he believes, because "dental hygiene is a modifiable risk factor. You can intervene to improve oral health." And, he pointed out, "our study areas in China and this region of Iran have the highest incidence of esophageal cancer in the world but have little else in common except limited alcohol and tobacco use."

Christian Abnet

Dr. Abnet plans to follow up these findings with a search for the biological mechanisms underlying the association between tooth loss and esophageal cancer risk. He is delighted with the possibilities offered by the NIH Roadmap Human Microbiome Project to explore this topic. Along with a postdoctoral research fellow, **Neal D. Freedman, Ph.D., M.P.H.** (NEB), Dr. Abnet is currently at work on a pilot study using saliva samples to study the contribution of oral flora to this association.



A drawing of a Wallace's Flying Frog *(Rhacophorus nigropalmatus)* by Christian Abnet

In another investigation of a large cohort of Chinese men and women, Dr. Abnet and his colleagues found an association between higher 25-hydroxyvitamin D (25[OH]D) serum concentrations and ESCC. This association appeared to be limited to males, however, and study participants exhibited serum 25(OH)D concentrations below the "normal" range. Dr. Abnet noted that when "esophageal squamous dysplasia (the precursor lesion to ESCC) was substituted as the end point, higher serum 25(OH)D was associated with higher risk of disease in both sexes. We'd like to see an association like this many times before we know it is meaningful, especially because vitamin D is currently a hot topic in cancer prevention." Dr. Abnet and his colleagues are working with the NCI Cohort Consortium to examine the potential association between higher serum 25(OH)D levels and ESCC across a range of populations. "This will allow us to examine groups with much higher vitamin D levels but will also include a population in Finland, where there is not as much sunlight as in the United States. Our previous results might be relevant only in the rural Chinese communities we were studying."

Using data collected as part of the Chinese cohort study, Dr. Abnet has expanded the use of x-ray fluorescence spectroscopy in epidemiologic studies to include direct measures of zinc concentrations in baseline tissue samples. He explained that "inadequate zinc has been clearly linked to esophageal cancer in elegant rodent studies, but this is difficult to examine in humans because of homeostasis and because zinc's bioavailability is strongly dependent on other food components." With biopsy specimens from the Chinese cohort and access to the powerful supercollider at Argonne National Laboratory, Dr. Abnet and his colleagues showed that hazard ratios for ESCC were significantly lower for subjects in the highest tissue zinc concentration quartile compared to those in the lowest quartile. "These are very valuable, prospective samples," Dr. Abnet said. "This study allowed us to use sections only five micrometers thick and examine zinc and four other elements as well. This got me really interested in assessing other nutritional and toxic elements in epidemiologic studies." He acknowledged that his work was the first to apply this technology in such a study and that others are also now using the tool.

Dr. Abnet finds a great deal of satisfaction in his contributions to NCI's mission to better understand the etiology and prevention of cancers. "My work advances knowledge just as much when working in China as when it involves Americans. NCI must go where the disease is." Outside of his work, Dr. Abnet enjoys drawing and spending time with his wife of 11 years, Dr. Rebecca Holden, and their two children, Clara, 10, and Soren, 7. ■

—Terry Taylor, M.A.

SPRING 2008 INTRAMURAL RESEARCH AWARD WINNERS

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

IRA Winners: Li Jiao, Dana Van Bemmel, and Rose Yang.

The winners of the spring 2008 competition were **Li Jiao, M.D., Ph.D.,** Nutritional Epidemiology Branch, for her proposal, "Advanced glycation end products, insulin resistance, and risk of colorectal cancer—A prospective case-cohort study"; **Dana M. Van Bemmel, Ph.D., M.P.H.,** Occupational and Environmental Epidemiology Branch, for "DNA hypomethylation and bladder cancer: A case analysis of the loss of heterozygosity on chromosome 9, aberrant global DNA methylation, and changes in epigenetic protein expression within the New England Bladder Cancer Study"; and **Rose Yang, Ph.D., M.P.H.,** Genetic Epidemiology Branch, for her proposal titled "Genome-wide search for copy number variants that are related to melanoma susceptibility in melanoma-prone families without known mutations."

Proposals were reviewed by members of the NCI Board of Scientific Counselors 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 time frame and resources, and relevance to the mission of the Division.

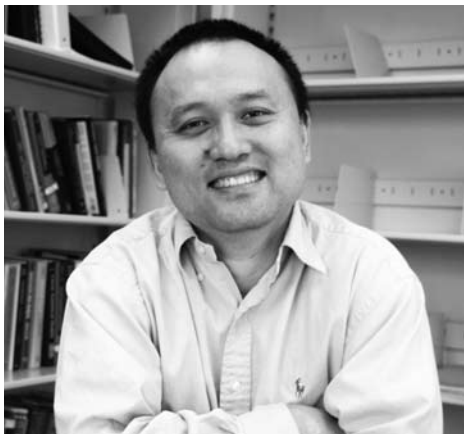
KAI YU LOVES TO SOLVE PROBLEMS

"It was really love at first sight," said **Kai Yu, Ph.D.,** referring to the first time he saw the advertisement for his present position as an investigator in the Biostatistics Branch (BB). "I wasn't even really looking. I was happy where I was, but I saw the job ad on the Internet, and it looked like the perfect opportunity."

Dr. Yu completed his M.S. in applied mathematics at the Beijing University of Posts and Telecommunications in China before coming to the United States to study computational engineering. He changed direction because he "found applied mathematics too confining. You tend to focus on one technique and apply it to any relevant question." Interested in biology but trained in mathematics, he combined the two disciplines, completing a Ph.D. in biostatistics at the University of Pittsburgh followed by postdoctoral work in statistical genetics at Stanford University.

Excited by rapid advances in medical technology and the development of large datasets, Dr. Yu saw statistical genetics as a very promising field. "I had little difficulty picking up the basics of genetics," Dr. Yu said. "There are a few fundamental rules, and everything flows from them. Besides," he chuckled, "one of the foundational concepts of genetics, the Hardy-Weinberg equilibrium, was first described by a mathematician."

His first contact at NCI in 2005 was **Sholom Wacholder, Ph.D.** (BB), who quickly confirmed Dr. Yu's initial impressions of the Institute as a place for groundbreaking research. Dr. Yu's conversations with Dr. Wacholder convinced him to leave his position in the School of Medicine at Washington



Kai Yu

University in St. Louis and join NCI. "Dr. Wacholder has become my mentor," said Dr. Yu. "I have worked with him on several projects and he is always extremely helpful. Of course my other colleagues in the branch are also very supportive."

What Dr. Yu loves about his work at NCI is the opportunity to work on high-impact projects. "You're not just working on abstract problems, but rather on something relevant to current research," he said. For example, he recently teamed up with investigators in the Cancer Genetic Markers of Susceptibility (CGEMS) project to study the impact of population stratification in genome-wide association studies (GWAS) with different control selection strategies.

Perhaps the most exciting of Dr. Yu's ongoing investigations is looking for ways to combine biological knowledge of genetic pathways and evidence from microarray studies with GWAS to uncover true genetic risk factors for cancer.

For this investigation, researchers generated two new studies using data from the CGEMS multistage studies of prostate and breast cancers. One combined the case data from the prostate cancer GWAS with control data from the breast cancer GWAS; the second used control data from the prostate cancer GWAS to compare with case data from the breast cancer GWAS. Analysis of the two original studies revealed very minor inflation of type I error when the cases were compared with their own controls. As expected, exchanging control groups increased this inflation factor. Dr. Yu and his colleagues developed a principal components selection procedure that allowed them to correct this inflation back to the original levels. As Dr. Yu explained, "our findings suggested that the reuse of controls from other studies can have acceptable type I error when a strategy to correct the effects of population satisfaction is employed. This opens the door to more cost-efficient GWAS with equally reliable results."

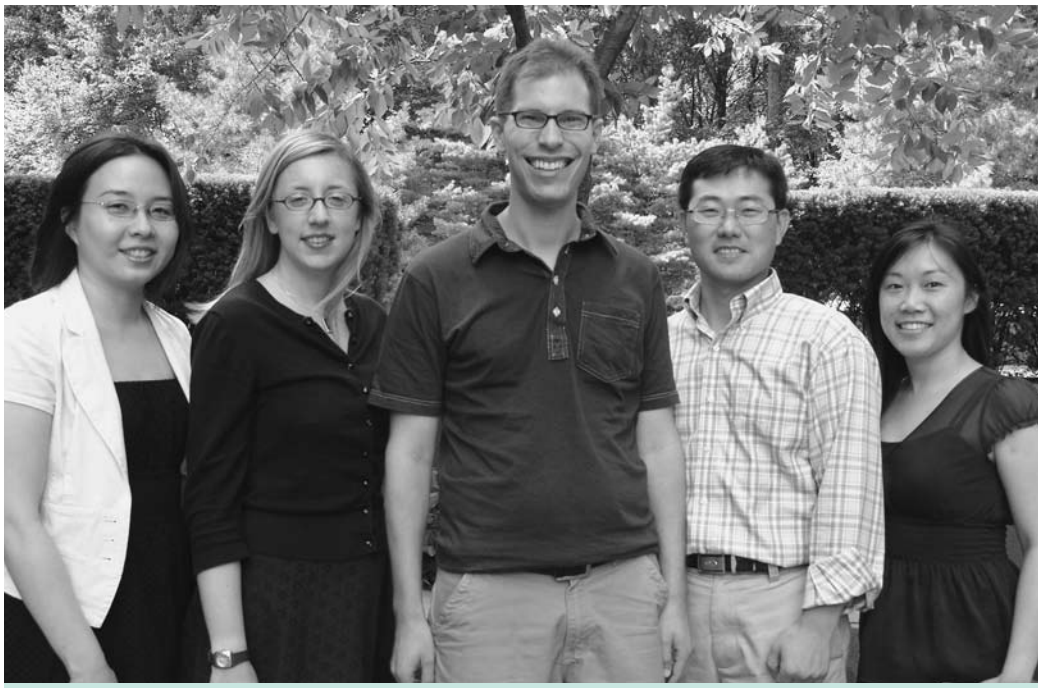
Dr. Yu has also explored new approaches to more effective correction of population stratification, working with a postdoctoral fellow, **Qizhai Li, Ph.D.** (BB). Using multidimensional scaling techniques, they uncovered both clustered and continuous patterns of population substructure and adjusted the data with improved strategies. "Currently, in carefully designed studies of European Americans, we don't see a big problem with population substructure," he explained. "For more diverse populations, this could become a real issue."

Explaining another of his recent investigations, Dr. Yu noted that "once you find a 'hit' (i.e., a single nucleotide polymorphism cancer association), you want to design a second study to replicate it, to see if your results are reliable. You need to know how big your sample should be and whether to combine data from the second study with those from the first." Dr. Yu and his colleagues used data from a published study of non-Hodgkin lymphoma to estimate the effect size for disease markers by a bootstrap procedure. "Because the naive estimate (the one observed from the first study) tends to be biased upward," Dr. Yu explained, "your power calculation gives a smaller sample size than actually needed." They showed that their estimates were more accurate, and their sample-size calculations gave power closer to the nominal level. They also concluded that reusing data from the first study is generally superior. "This study is an important first step toward a solution to this question," Dr. Yu said.

Perhaps the most exciting of Dr. Yu's ongoing investigations is looking for ways to combine biological knowledge of genetic pathways and evidence from microarray studies with GWAS to uncover true genetic risk factors for cancer. Dr. Yu believes it is critical to better incorporate existing knowledge of the disease into the gene-finding algorithm. "We need a better, more powerful algorithm guided by existing knowledge that can search the entire space of all possible models more intelligently."

"I love solving problems," he said. "The good thing about my work here at NCI is that problem solving can have a direct impact on public health." ■

—Terry Taylor, M.A.



FARE Winners: Chu-Ling Yu, Gwen Murphy, Neal Freedman, Kyoung-Mu Lee, and Linda Dong.

NIH RECOGNIZES 2009 FARE WINNERS

The NIH Fellows Award for Research Excellence (FARE) program recognizes scientific research by intramural postdoctoral fellows. Fellows submit abstracts of their research, which are reviewed by a panel of NIH postdoctoral fellows and principal investigators. Winners receive a $1,000 travel stipend to attend and present their work at a scientific meeting. This year, 1,045 applications were received from fellows across NIH. Of 274 winning abstracts, 5 were from DCEG fellows.

DCEG Winners and Abstract Titles

- **Linda Dong, Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB): *Comprehensive analysis of candidate growth, differentiation, and apoptosis genes with risk of renal cancer in the Central and Eastern European Renal Cancer Study.*
- **Neal D. Freedman, Ph.D., M.P.H.,** Nutritional Epidemiology Branch: *Cigarette smoking and subsequent risk of lung carcinoma in men and women.*
- **Kyoung-Mu Lee, Ph.D.** (OEEB): *Differential effects of smoking and smoky coal use on lung cancer mortality before and after chimney installment in Xuanwei, China.*
- **Gwen Murphy, Ph.D., M.P.H.,** Infections and Immunoepidemiology Branch: *Epstein-Barr virus and gastric adenocarcinoma: A meta-analysis.*
- **Chu-Ling Yu, Sc.D.,** Radiation Epidemiology Branch: *Assessment of lifetime cumulative sun exposure using self-administered questionnaire: Reproducibility of two approaches.*

More information about the FARE competition is available at http://felcom.nih.gov/FARE.

INAUGURAL MEETING OF THYGENE CONSORTIUM

In June, the first meeting of the Thyroid Cancer Genetics and Epidemiology (THYGENE) consortium was held in Rockville. Organized by **Alice J. Sigurdson, Ph.D.,** Radiation Epidemiology Branch (REB), and Dr. Erich Sturgis from the University of Texas M.D. Anderson Cancer Center, the meeting's primary goals were to facilitate pooling of existing genetic data and to identify genetic markers and epidemiologic risk factors for thyroid cancer.

First thyroid cancer meeting participants

The THYGENE consortium includes more than 16 study centers from around the world, and 29 researchers from eight countries attended the meeting. Participants discussed short- and long-term projects to uncover novel thyroid cancer susceptibility loci and to assess possible effect modification by environmental factors, including radiation exposure. Other co-organizers and participants from DCEG included **Parveen Bhatti, Ph.D., Houda Boukheris, M.D., Ph.D., Alina V. Brenner, M.D., Ph.D., Maureen C. Hatch, Ph.D.,** and **Elaine Ron, Ph.D., M.P.H.** (all of REB); **Ruth M. Pfeiffer, Ph.D.,** Biostatistics Branch (BB); and **Jeffrey Yuenger, M.S.,** Core Genotyping Facility.

The next day, DCEG scientists Dr. Ron, **Jay H. Lubin, Ph.D.** (BB), and **Lene Veiga, Ph.D.** (REB), led the first meeting of the Pooled International Radiation and Thyroid Cancer Epidemiology Studies (PIRATES) group. The purpose of the meeting was to present and discuss the study protocol, determine data-sharing policies, and develop a timetable. The study will expand upon a 1995 analysis of radiation-associated thyroid cancers by Drs. Ron and Lubin, which pooled data from seven studies. The current project will be based on 15 studies conducted in Europe, Asia, and the United States. In total, PIRATES will include data on more than 160,000 exposed subjects and about 2,000 thyroid cancer cases. The study will focus on quantifying the thyroid cancer risk associated with adult radiation exposure, gender, attained age, and time since exposure. It will evaluate risk by histologic type, describe the shape of the dose-response curve, and compare the effects of acute and fractionated doses. Participants from DCEG were Dr. Bhatti, Dr. Brenner, Dr. Sigurdson, **Kwang Pyo Kim, Ph.D., Ruth A. Kleinerman, M.P.H., Charles E. Land, Ph.D.** (all of REB), and **Margaret A. Tucker, M.D.,** Director of the Human Genetics Program and Chief of the Genetic Epidemiology Branch. ■

—Elaine Ron, Ph.D., M.P.H., Alice J. Sigurdson, Ph.D., and Lene Veiga, Ph.D.

MONOGRAPH ON FAMILIAL CANCER SYNDROMES PUBLISHED

Mark H. Greene, M.D., Chief of the Clinical Genetics Branch, **Mary Lou McMaster, M.D.,** Genetic Epidemiology Branch, Dr. Carl J. Lindor, and Dr. Noralane M. Lindor, both from the Mayo Clinic in Rochester, Minnesota, have coauthored the second edition of the *Concise Handbook of Familial Cancer Susceptibility Syndromes.* The first edition, published about 10 years ago, was a unique compendium and an essential guide for oncologists, clinical geneticists, cancer genetic counselors, and genetic nurses who cared for families with hereditary cancer predisposition syndromes. With rapid advances in the fields of cancer genetics, genomics, and molecular epidemiology, the need for a new edition became more pressing by the year. The authors worked hard to ensure that the second edition would be a practical tool for daily clinical practice.

The updated handbook includes more topics (from 35 to 55 disorders) as well as two new tabular summaries to aid in diagnosis. The tables include the benign neoplasms and other clinical manifestations associated with specific cancer susceptibility disorders.

—June A. Peters, M.S., C.G.C.

AN UPDATE ON THE INTERLYMPH CONSORTIUM

InterLymph meeting participants

The InterLymph Seventh Annual Meeting and a preceding one-day symposium, titled "New Insights into the Causes of Lymphoma," were held July 28 to 31 in Sydney, Australia. The symposium included sessions with talks sponsored by the six InterLymph Working Groups. Presentations were given by four DCEG investigators, **Ola Landgren, M.D., Ph.D.,** Genetic Epidemiology Branch, **Mark Purdue, Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB), **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (OEEB), and **Sophia S. Wang, Ph.D.,** Hormonal and Reproductive Epidemiology Branch, on the role of lifestyle, environmental, and occupational risk factors and candidate genetic loci in relation to risk of non-Hodgkin lymphoma (NHL). The InterLymph Coordinating Committee, including **Martha S. Linet, M.D., M.P.H.,** Chief of the Radiation Epidemiology Branch, organized the symposium, which was attended by researchers from 11 countries as well as local hematologists, oncologists, and pathologists.

The collaborations by InterLymph members have to date resulted in 12 pooled analyses of lifestyle, environmental, familial, and genetic factors and risk of NHL. The annual meeting included sessions for working groups to plan and develop future research efforts. New proposals were presented to assess the modifying role of specific gene variants on the risks associated with hair dye use, smoking, ultraviolet radiation, obesity, hepatitis C, autoimmune disorders, and other factors. A second area of emphasis will be comprehensive assessment of risk factors for rare NHL subtypes, including mantle cell, peripheral T-cell, and t(14;18). Other NHL subtypes of interest include marginal zone group (MALT); splenic, nodal, and cutaneous lymphomas; acute lymphoblastic leukemia/lymphoma; and Burkitt lymphoma/leukemia. A third initiative will focus on improving the types of information about lymphomas that are collected by population-based cancer registries.

Two major efforts will be launched during the coming year to facilitate InterLymph initiatives. A survey will be administered to identify the numbers of cases within the consortium with specific histopathological subtypes, the genotyping efforts and specific pathways that have been examined in individual studies, and the specific variables evaluated in each study. In addition, a data coordination center will be established to provide centralized, well-documented approaches for combining datasets; create a comprehensive data dictionary; develop core variables; and provide assistance and guidance on the more complex statistical analyses to be undertaken.

The symposium was attended by InterLymph researchers from 11 countries as well as local hematologists, oncologists, and pathologists.

The meeting was held at the historic and architecturally unique Royal Australasian College of Physicians, adjacent to the Sydney Botanic Gardens. The superb organization by hosts Dr. Andrew Grulich and Dr. Claire Vajdic from the University of New South Wales resulted in an exciting and highly productive experience for all participants. The next InterLymph meeting, to be held at the University of British Columbia in Vancouver, Canada, will be hosted by Dr. John Spinelli and Dr. Angela Brooks-Wilson from the British Columbia Cancer Research Centre. ■

—Annelie M. Landgren, M.P.H.

2008 DCEG SUMMER FELLOWS

DCEG summer fellowships continue to provide bright and dedicated students with invaluable experience conducting cancer epidemiology and genetics research. This year DCEG accepted 29 students, making this the largest group of summer fellows to date.

Students worked on a range of research projects and presented their findings at the Tenth Annual DCEG Summer Recognition and Poster Event, organized by **Kristin Kiser, M.H.A.,** Fellowship Program Coordinator in the Office of Education (OE). The event featured posters by 16 students, who also participated in the NIH Summer Student Poster Session. A recognition ceremony and discussion with **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, **Shelia Hoar Zahm, Sc.D.,** DCEG Deputy Director, and **Jackie Lavigne, Ph.D., M.P.H.,** Chief of OE, concluded the day.

Students interested in applying for 2009 summer fellowships at DCEG may submit an application to the NIH Summer Application site (www.training.nih.gov/student/index.asp) starting in mid-November. Students with a specific interest in cancer epidemiology and genetics are encouraged to learn more about DCEG research and complete a supplemental application at http://dceg.cancer.gov/fellowships/summerprogram.

DCEG summer fellows and mentors

Reflections from 2008 DCEG Summer Fellows

"This summer has been terrific! The summer fellowship isn't just a way of doing hands-on projects, but also it provides an opportunity for networking with other students and investigators, learning how the Division operates and how scientists apply their knowledge to different projects and their lifestyles. The mentors here are the best of the best."

–Katherine Lin

"I especially enjoyed the poster presentations at DCEG as I was able to share the knowledge I gained from my lab while learning from other students about the research they were involved in over the summer. This new knowledge helped me see that the genotyping I was performing was truly helping the various cancer studies occurring across DCEG."

–Hiren Mistry

"I appreciated the guidance of my mentors because without their enthusiasm, I wouldn't have learned as much as I did. I enjoyed being part of the research that I know will continue after I leave, and I'm glad that I have made a contribution."

–Julia Tse

"My summer here at NIH has truly been a unique and enriching learning experience. It's such an amazing place with lots of intellectual candy to nibble on."

–Tanya Vacharkulksemsuk

"This summer internship was an unforgettable experience, and I plan on coming back next summer to continue this exciting research!"

–Alexander Fischer

"I have really enjoyed my work experience here at NCI, and the work I have done this past summer has really opened my eyes to a very intriguing career field."

–Dara Khatib ■

—Kristin Kiser, M.H.A.

KOUTROS WINS STUDENT PRIZE

Stella Koutros presents her recent paper.

Stella Koutros, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB), received the 2008 Student Prize from the American College of Epidemiology (ACE) for her paper, "Aromatic amine pesticide use and human cancer risk: Results from the U.S. Agricultural Health Study." Completed with mentoring from **Michael C.R. Alavanja, Dr.P.H.** (OEEB), and Dr. Tongzhang Zheng of Yale University, the paper was part of her doctoral thesis. The award included funds for travel to the ACE annual meeting, where she gave a plenary presentation and was presented with the award.

DCEG SUMMER FELLOWS AND THEIR MENTORS

Priya Baliga, George Washington University School of Public Health and Health Services. Mentor: **Maureen C. Hatch, Ph.D.** (Radiation Epidemiology Branch [REB])

Madeleine Blank, University of Michigan School of Public Health. Mentor: **Yikyung Park, Sc.D.** (Nutritional Epidemiology Branch [NEB])

Amanda Bowes, Bryn Mawr College. Mentor: **Ruth A. Kleinerman, M.P.H.** (REB)

Jacob Calcei, Kenyon College. Mentor: **Jesus Gonzalez-Bosquet, M.D., Ph.D.** (Laboratory of Translational Genomics [LTG])

Maria C. Camargo, University of Illinois at Chicago. Mentors: **Charles S. Rabkin, M.D.,** and **Hui-Lee Wong, Ph.D.** (Infections and Immunoepidemiology Branch [IIB])

Cyril William Draffin, Winston Churchill High School. Mentors: **Jun Fang, M.D., Ph.D.,** and **Laufey Amundadottir, Ph.D.** (LTG)

Alexander Fischer, University of Maryland, College Park. Mentor: **Dalsu Baris, M.D., Ph.D.** (Occupational and Environmental Epidemiology Branch [OEEB])

Allison Gathany, Yale University School of Public Health. Mentor: **Sophia S. Wang, Ph.D.** (Hormonal and Reproductive Epidemiology Branch [HREB])

Alison Glassman, Florida State University. Mentor: Dr. Park

Matthew Herman, Washington University in St. Louis. Mentors: **Jorge R. Toro, M.D.** (Genetic Epidemiology Branch), and Ming-Hui Wei (SAIC)

Sarah Kramer, Walt Whitman High School. Mentor: Dr. Amundadottir

Katherine Lin, Johns Hopkins University Bloomberg School of Public Health. Mentors: **Mary H. Ward, Ph.D.** (OEEB), and **Sonya Heltshe, Ph.D.** (Biostatistics Branch [BB])

Jacqueline Major, University of California, San Diego. Mentor: **Demetrius Albanes, M.D.** (NEB)

Christina McIntosh, Spelman College. Mentors: **Philip S. Rosenberg, Ph.D.,** and **William F. Anderson, M.D., M.P.H.** (BB)

Alison Meisner, University of Connecticut. Mentors: Dr. Rosenberg and **Lee E. Moore, Ph.D.** (OEEB)

Samantha Miner, Middletown High School. Mentor: **Allan Hildesheim, Ph.D.** (IIB)

Hiren Mistry, Richard Montgomery High School. Mentor: **Amy Hutchinson, M.S.** (Core Genotyping Facility)

Julia Molony, University of Minnesota Graduate School. Mentor: **Ethel S. Gilbert, Ph.D.** (REB)

Brietta Oaks, George Washington University School of Public Health and Health Services. Mentor: **Rachael Z. Stolzenberg-Solomon, M.P.H., Ph.D.** (NEB)

Leah Pedoeim, Charles E. Smith Jewish Day School, and **Dara Khatib,** Winston Churchill High School. Mentor: **Farin Kamangar, M.D., Ph.D.** (NEB)

Jessica Rinsky, University of Kentucky College of Public Health. Mentor: Dr. Moore

Jamie Ritchey, University of South Carolina School of Public Health. Mentor: **Ann W. Hsing, Ph.D.** (HREB)

Anushi Shah, Syracuse University. Mentors: **Sam M. Mbulaiteye, M.D.,** and **Mercy Guech-Ongey, Ph.D.** (IIB)

Julia Tse, Dartmouth College. Mentor: Dr. Anderson

Tanya Vacharkulksemsuk, University of North Carolina at Chapel Hill. Mentor: **June A. Peters, M.S., C.G.C.** (Clinical Genetics Branch [CGB])

Aaron Wacholder, Stanford University. Mentor: **Liudimla Prokunina-Olsson, Ph.D.** (LTG)

Sarah Weinstein, University of Buffalo School of Medicine and Biomedical Sciences. Mentor: **Neelam Giri, M.D.** (CGB)

Sara Wichner, University of Chicago. Mentor: **Peter D. Inskip, Sc.D.** (REB)

CONSORTIUM WILL FOCUS ON ESOPHAGEAL DISEASE IN ASIA

International collaborations in clinical and epidemiologic research on esophageal adenocarcinoma and its precursor, Barrett's esophagus, reached a new milestone in May with the formation of the Asian Barrett's Consortium (ABC). Although the rapid increases of these diseases have been noted in Western countries for more than three decades, their occurrence in Asia has been reported only recently and may signal an early stage of a similar epidemic. As many of the Asian countries have experienced recent, rapid environmental, socioeconomic, and lifestyle changes, this region may provide a unique opportunity for research into the initiating factors for Barrett's esophagus and esophageal adenocarcinoma.

Asian Barrett's Workshop organizers and speakers

DCEG, along with the Division of Cancer Control and Population Sciences, Division of Cancer Prevention, and the NIH Office of Rare Diseases, hosted an Asian Barrett's Workshop, chaired by **Wong-Ho Chow, Ph.D.,** Occupational and Environmental Epidemiology Branch, **Sanford M. Dawsey, M.D.,** Nutritional Epidemiology Branch (NEB), and Dr. Emad El-Omar from the University of Aberdeen, United Kingdom. The workshop was attended by clinical investigators from China, Hong Kong, India, Japan, Singapore, South Korea, and Taiwan as well as by invited experts from Sweden, the United Kingdom, and the United States. Recognizing the emergence of Barrett's esophagus and esophageal adenocarcinoma in Asia and the potential for more powerful research with pooled resources and expertise, the workshop participants formed a consortium to continue the dialogue and to plan future collaborative research projects. Modeled after the successful Barrett's Esophagus and Adenocarcinoma Consortium (BEACON), the ABC has several working groups, focusing on endoscopy, pathology, epidemiology, and protocol development, as well as a steering committee chaired by Dr. Lawrence Khek-Yu Ho from the National University of Singapore. A proof-of-principle study of interobserver reliability of endoscopy diagnosis is being planned by Dr. Prateek Sharma from the University of Kansas School of Medicine with support from **Michael B. Cook, Ph.D.,** Hormonal and Reproductive Epidemiology Branch.

We look forward to seeing the consortium blaze the trail to uncovering many clues that will help us take meaningful steps toward intervening on this potentially malignant disease.

May also marked the third annual meeting of BEACON, a consortium of studies from Western countries established at a similar workshop chaired by Dr. Chow, Dr. Olof Nyrén from Karolinska University in Sweden, and Dr. Thomas Vaughan from the Fred Hutchinson Cancer Research Center. To date, the consortium has received grants from NIH, Cancer Research UK, and the Swedish Cancer Board. With **Farin Kamangar, M.D., Ph.D.** (NEB), leading the effort, a database of approximately 22,000 cases and controls has been established. Several manuscripts are in preparation, and new projects were discussed and planned.

Dr. Chow credits the success of BEACON to the collegial spirit of the members, their generosity in donating time and study resources, and the exemplary leadership of the current chair, Dr. Vaughan. She also expressed confidence that the ABC will become an equally successful and productive consortium. The ABC chair, Dr. Ho, noted: "As we take our first stride in this endeavor, we look forward to seeing the consortium blaze the trail to uncovering many clues that will help us take meaningful steps toward intervening on this potentially malignant disease." ■

—Wong-Ho Chow, Ph.D., and Farin Kamangar, M.D., Ph.D.

RECENT NEWSLETTERS ON FAMILIAL CANCER RESEARCH

Families that share genetic mutations, particularly those that may lead to cancer, make important contributions to our knowledge of cancer when they participate in clinical trials. The Genetic Epidemiology Branch (GEB) and Clinical Genetics Branch (CGB) regularly prepare newsletters to inform study participants of research progress and related information.

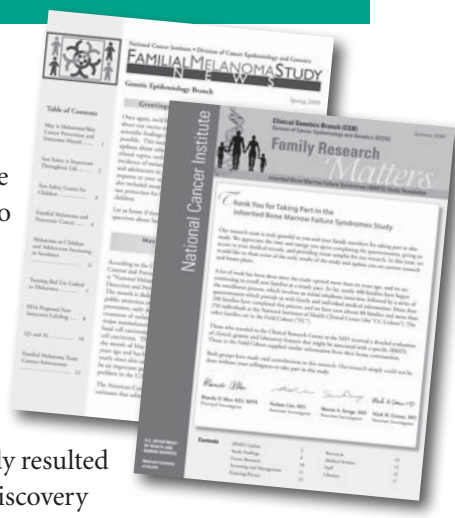
GEB, which has been studying families with multiple cases of cutaneous melanoma for more than three decades, recently mailed a new edition of the Familial Melanoma Study Newsletter to approximately 2,000 study participants. The newsletter focused on the importance of lifelong sun safety, highlighting exposure to ultraviolet light as the primary modifiable risk factor for melanoma and non-melanoma skin cancers.

The newsletter summarized an article reporting an excess of pancreatic cancer observed among a subset of the study families, some of whom have mutations in *CDKN2A,* a documented melanoma susceptibility gene. However, there are no recognized genetic or other factors that identify which, if any, family members may be at increased risk of developing pancreatic cancer. Branch investigators are actively working on answering this question. Resources for further information about pancreatic cancer were also included.

Other articles included a consensus report by the International Agency for Research on Cancer on its recent review showing that tanning bed use during the teenage years and twenties is associated with an increased risk of melanoma and squamous cell skin cancer; an article on the FDA's proposed new sunscreen labeling regulations; and a discussion of the increasing incidence of melanoma among adolescents and young adults observed in the NCI Surveillance, Epidemiology, and End Results (SEER) database.

In addition, CGB recently published the first issue of its newsletter for participants in the Inherited Bone Marrow Failure Syndromes (IBMFS) Study, summarizing activities since the study opened in January 2002. The newsletter outlined the clinical, laboratory, and genetic information and the risks of malignancies (leukemia and solid tumors) for each of the component disorders in IBMFS: Fanconi anemia, dyskeratosis congenita (DC), Diamond-Blackfan anemia, Shwachman-Diamond syndrome, severe congenital neutropenia, amegakaryocytic thrombocytopenia, and thrombocytopenia with absent radii.

Major findings from IBMFS related to DC were also highlighted in the newsletter. DCEG researchers were the first to show that patients with DC could be identified by abnormally short telomeres in white blood cell subsets, an innovation that led to reclassification of several patients with aplastic anemia who were initially thought to have an acquired, not genetic, disease. Adding telomere length to the case definition for an NCI genetic linkage study resulted in the discovery of a new gene for the syndrome, *TINF2*. Mutations are more common in this gene than in any genes previously found to be associated with DC.



The newsletter included general and syndrome-specific recommendations for screening and management of these rare disorders as well as an extensive glossary of relevant medical terminology. It was mailed to nearly 700 study participants ages 18 and older, pediatric hematology/oncology specialists, and genetic counselors who focus on oncology and prenatal genetics. ■

—Mary C. Fraser, R.N., M.A., and Blanche P. Alter, M.D., M.P.H.

ZAHM RECEIVES HARVARD SCHOOL OF PUBLIC HEALTH ALUMNI AWARD OF MERIT

In June, **Shelia Hoar Zahm, Sc.D.,** Deputy Director of DCEG, received the Harvard School of Public Health Alumni Award of Merit for her research on occupational and environmental cancer as well as her outstanding scientific leadership and community service. This award, the highest honor presented to alumni by the Harvard School of Public Health, recognizes leaders who advance the science of public health, improve its community practice, provide exceptional leadership of public health institutions, or contribute significantly to the training and accomplishments of the field's future professionals.

Shelia Zahm receives Harvard Alumni of Merit Award from Dean Barry Bloom.

DCEG STAFF WIN NIH MERIT AWARDS

At the annual NIH Awards Ceremony in October, NCI Director John E. Niederhuber, M.D., presented NIH Merit Awards to the following DCEG staff members in recognition of their accomplishments:

Mark E. Sherman, M.D., Hormonal and Reproductive Epidemiology Branch (HREB), for his leadership in incorporating molecular pathology components into epidemiologic investigations of breast and gynecologic malignancies, helping those studies provide unique etiologic insights.

Rachael Z. Stolzenberg-Solomon, M.P.H., Ph.D., Nutritional Epidemiology Branch (NEB), for her sustained and innovative work in elucidating nutritional, genetic, infectious, and other determinants of pancreatic cancer.

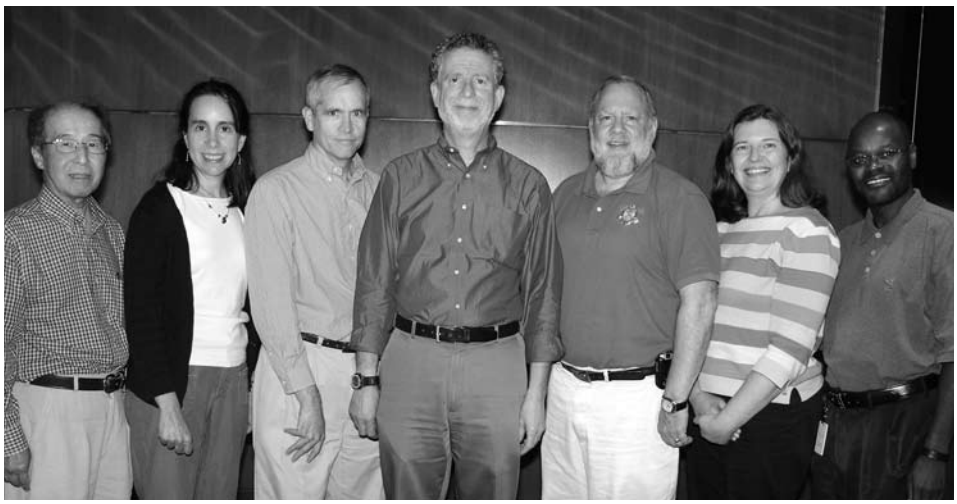
William F. Anderson, M.D., M.P.H., Biostatistics Branch (BB), for providing new insights into cancer etiology through descriptive studies of cancer heterogeneity and racial disparities and for innovative use of the SEER Residual Tissue Repository.

Mark H. Greene, M.D., Chief of the Clinical Genetics Branch (CGB), for his leadership in forming GOG-0199, a unique intramural/extramural collaboration that creates a national research resource.

Sam M. Mbulaiteye, M.D., Infections and Immunoepidemiology Branch (IIB), for developing an innovative program of research in Kaposi sarcoma, non-Hodgkin lymphoma, and other malignancies in Uganda.

Kiyohiko Mabuchi, M.D., Dr.P.H., Radiation Epidemiology Branch (REB), for his long-standing contributions to a continuing cohort study of atomic bomb survivors, which has provided epidemiological insights into long-term cancer risk from radiation and other exposures.

Group Merit Winners: (front) Rose Yang, Jill Koshiol, Farin Kamangar, Gabriella Andreotti, Ann Hsing, Louise Brinton, Maureen Hatch, Wong-Ho Chow, Christian Abnet, Philip Taylor, and Susan Privot; (back) James Goedert, Mark Sherman, Philip Rosenberg, Neal Freedman, and Mark Roth. (Not shown: Michael Alavanja, Aaron Blair, Stephen Chanock, Sanford Dawsey, Joseph Fraumeni, Montserrat García-Closas, Larissa Korde, and Patricia Stewart.)



Individual Merit Winners: Kiyohiko Mabuchi, Rachael Stolzenberg-Solomon, William Anderson, Arthur Schatzkin, Mark Greene, Kristin Kiser, and Sam Mbulaiteye. (Not shown: Mark Sherman.)

Arthur Schatzkin, M.D., Dr.P.H., Chief of NEB, for his research, mentoring, and direction of the Branch.

Kristin Kiser, M.H.A., Office of Education (OE), for her leadership in facilitating DCEG's annual training related to the U.S. Public Health Service Policy on Instruction in the Responsible Conduct of Research.

The NCI-Shanghai Biliary Tract Cancer Study investigators: **Stephen J. Chanock, M.D.,** Director of the Core Genotyping

Facility and Chief of the Laboratory of Translational Genomics, **Gabriella Andreotti, Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB), **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, **Ann W. Hsing, Ph.D.** (HREB), Shelley Niwa (Westat), and **Philip S. Rosenberg, Ph.D.** (BB), for notable discoveries that have elucidated lifestyle and genetic risk factors for biliary tract cancer.

The Multidisciplinary Study of Breast, Endometrial, and Ovarian Cancers in Poland team: **Aaron E. Blair, Ph.D., M.P.H.** (OEEB), **Louise A. Brinton, Ph.D.,** Chief of HREB, Dr. Chanock, **Montserrat García-Closas, M.D., Dr.P.H.** (HREB), Dr. Sherman, **Patricia Stewart, Ph.D.** (OEEB), and **Rose Yang, Ph.D., M.P.H.,** Genetic Epidemiology Branch (GEB), for successfully conducting a multidisciplinary study of breast, endometrial, and ovarian cancers in Poland that enabled new insights into the etiologic heterogeneity of these tumors.

The NCI Special Studies Institutional Review Board (SSIRB) members: **Michael C.R. Alavanja, Dr.P.H.** (OEEB), **James J. Goedert, M.D.** (IIB), **Maureen C. Hatch, Ph.D.** (REB and Chair of SSIRB), **Larissa A. Korde, M.D., M.P.H.** (CGB), and **Susan Privot,** Office of the Director, along with Joan L. Becker (NCI Division of Cancer Control and Population Sciences [DCCPS]), Dr. Michael Greene, Dr. Sarah C. Kobrin (DCCPS), Dr. Celia Maxwell (Howard University), Dr. Isis S. Mikhail (DCCPS), Dr. Nancy A. Potischman (DCCPS), Lynn Sayers, and Jack Schwartz (Maryland Attorney General's Office), for developing new policies for protocol review that address the human subject considerations specific to genome-wide association studies.

The DCEG Upper Gastrointestinal Tract Cancers Research Group: **Christian C. Abnet, Ph.D., M.P.H.** (NEB), **Wong-Ho Chow, Ph.D.** (OEEB), **Sanford M. Dawsey, M.D.** (NEB), **Neal D. Freedman, Ph.D., M.P.H.** (NEB), **Farin Kamangar, M.D., Ph.D.** (NEB), **Jill Koshiol, Ph.D.** (GEB), **Mark J. Roth, M.D.** (NEB), and **Philip R. Taylor, M.D., Sc.D.** (GEB), for 25 years of leadership in research on the etiology, early detection, and prevention of upper gastrointestinal tract cancers.

In addition, **Jackie Lavigne, Ph.D., M.P.H.,** Chief of OE, received an NCI Outstanding Mentor Award for her contribution to a critical element of DCEG's mission—training the next generation of scientists. **Richard B. Hayes, D.D.S., Ph.D.** (OEEB), received a Mentor of Merit Award.

Barry I. Graubard, Ph.D. (BB), **Qing Lan, M.D., Ph.D., M.P.H.** (OEEB), and Dr. Taylor were Outstanding Mentor Merit Award nominees. Nominations for these awards are written by NCI postdoctoral fellows. ■

INVESTIGATORS NEWLY AWARDED TENURE

NIH recently awarded scientific tenure to **Sophia S. Wang, Ph.D.,** of the Hormonal and Reproductive Epidemiology Branch (HREB), and **Mary H. Ward, Ph.D.,** of the Occupational and Environmental Epidemiology Branch (OEEB).

Mary Ward and Sophia Wang

Dr. Wang joined HREB as a tenure-track investigator in 2000 after receiving a doctorate in epidemiology from the Johns Hopkins Bloomberg School of Public Health and serving as a CDC Epidemic Intelligence Service Officer. Her research has focused on understanding the molecular pathogenesis and genetic susceptibility of cervical cancer and non-Hodgkin lymphoma (NHL). In her cervical cancer research, she is delineating the genetic and molecular events necessary for each progressive disease stage. In her NHL research, she investigates the role of genetic susceptibility factors and gene-environment interactions in NHL and NHL subtypes.

Dr. Ward began her career at DCEG as a doctoral student at Johns Hopkins, conducting her thesis research within OEEB. After receiving her degree in epidemiology, Dr. Ward stayed in the Branch as a postdoctoral fellow and became a tenure-track investigator in 1999. She has investigated the role of nitrate and nitrite from drinking water and dietary sources on cancer risk, using environmental monitoring data and geographic information systems to assess exposures. She also initiated interdisciplinary collaborations with experts in remote sensing, geospatial science, and environmental engineering to develop new methods to assess exposure to agricultural pesticides. She has applied these methods in case-control studies of NHL and childhood leukemia.

COMMITTEE OF SCIENTISTS UPDATE

The Committee of Scientists (COS) recently completed analysis of its 2008 survey of DCEG scientists. The role of the COS is to advise the Office of the Director (OD) about issues, challenges, and concerns relevant to the DCEG scientific staff and to facilitate communication across the Division at all scientific levels. This year's questionnaire included 74 questions, designed to assess six critical aspects of the work environment: administration and operations; travel; personnel; recruitment; scientific environment; and facilities and infrastructure. There was a 50% response rate, and the distribution of respondents by position was 29% fellows, 17% staff scientists/clinicians, 8% tenure-track investigators, 24% senior investigators/experts, and 22% unspecified.

Members of the COS met with **Joseph F. Fraumeni, Jr., M.D.,** Division Director, **Shelia Hoar Zahm, Sc.D.,** Deputy Division Director, **Jackie Lavigne, Ph.D., M.P.H.,** Chief of the Office of Education, and **Marianne K. Henderson, M.S.,** Chief of the Office of Division Operations and Analysis, to discuss the survey results and make recommendations. The results indicated that, overall, DCEG researchers are very satisfied with the opportunities afforded to them through the Division to pursue high-quality research. Some of the areas identified as inhibiting their ability to work efficiently are external to Division control, such as the technology transfer process, extensive training requirements, travel restrictions, and new personnel review requirements. Drs. Fraumeni and Zahm are committed to providing support to help the Division address these various requirements while preserving a high-quality research environment. Survey respondents would like to take more active roles in recruitment and in discussions about the scientific direction for the Division. Respondents also indicated a desire for more information on personnel reviews, Performance Management Appraisal Plan (PMAP) ratings, and salary determination. In response to these concerns, the COS suggested that the OD provide the branches with periodic updates about these processes and other aspects of Division operations.

Lastly, committee members discussed whether additional travel funds should be supplied for Division fellows to attend professional meetings and gain experience in presenting their work. Division policy is that each fellow is allotted one trip per year. There are opportunities for additional trips through the NIH Fellows Award for Research Excellence (FARE) program and the similar DCEG DFARE travel award program. The survey responses and COS recommendations will be taken into consideration by Division leadership to revise current operations in accordance with the mission of DCEG.

Barry Graubard and Katherine McGlynn

More information about the COS is available at http://intranet.dceg.cancer.gov/committees/cos/charter.html. ■

—Barry I. Graubard, Ph.D.

Several members of the COS will complete their terms this year. Outgoing members are: chair **Barry I. Graubard, Ph.D.,** Biostatistics Branch (BB); **Wong-Ho Chow, Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB); **Eric A. Engels, M.D., M.P.H.,** Infections and Immunoepidemiology Branch (IIB); **Neal D. Freedman, Ph.D., M.P.H.,** Nutritional Epidemiology Branch (NEB); **Kwang Pyo Kim, Ph.D.,** Radiation Epidemiology Branch (REB); **Jill Koshiol, Ph.D.,** Genetic Epidemiology Branch (GEB); and **Phuong Mai, M.D.,** Clinical Genetics Branch (CGB).

Representing each of the branches, current members are: chair **Katherine A. McGlynn, Ph.D., M.P.H.,** Hormonal and Reproductive Epidemiology Branch (HREB); **Christian C. Abnet, Ph.D., M.P.H.** (NEB); **Alina V. Brenner, M.D., Ph.D.** (REB); **Kenneth P. Cantor, Ph.D., M.P.H.** (OEEB); **Ying Gao, M.D., Ph.D., M.P.H.** (GEB); **James J. Goedert, M.D.** (IIB); **Lindsey M. Hoskins, M.S., L.G.M.F.T.** (CGB); **Ann W. Hsing, Ph.D.** (HREB), who serves as *Ex Officio* Women Scientist Advisor Committee Member; **Hormuzd A. Katki, Ph.D.** (BB); and **Kristin Kiser, M.H.A.,** Office of Education (Executive Secretary).

SCIENTIFIC HIGHLIGHTS

BILIARY TRACT CANCER

Gene Variants

The authors evaluated 62 single nucleotide polymorphisms (SNPs) in 22 inflammation-related genes in relation to biliary tract cancer and gallstones in a population-based case-control study conducted in Shanghai, China. The study included 411 cases with biliary tract cancer (237 gallbladder, 127 extrahepatic bile duct, and 47 ampulla of Vater), 895 with biliary stones, and 786 controls. Fourteen SNPs were related to the risk of biliary cancer and stones. Variants in the *IL8, IL8RB, RNASEL,* and *NOS2* genes were associated with biliary stones, whereas *VEGF* variants were associated with gallbladder cancer. Among the 10 genes with multiple SNPs from which haplotypes were inferred, only 1 *IL8RB* haplotype, consisting of 3 SNPs (rs2230054, rs1126579, and rs1126580), was associated with the risk of bile duct cancer and biliary stones, relative to the most frequent haplotype. Common variants in genes that influence inflammatory responses may predispose to gallstones and biliary tract cancer, suggesting the need for studies on the immunologic and inflammatory pathways that contribute to biliary diseases, including cancer. **(Hsing AW, Sakoda LC, Rashid A, Andreotti G, Chen J, Wang BS, Shen MC, Chen BE, Rosenberg PS, Zhang M, Niwa S, Chu L, Welch R, Yeager M, Fraumeni JF Jr, Gao YT, Chanock SJ. Variants in inflammation genes and the risk of biliary tract cancers and stones: A population-based study in China. *Cancer Res* 2008;68:6442–6452)**

In the same study population, five SNPs in four DNA repair genes (*MGMT, RAD23B, CCNH,* and *XRCC3*) were evaluated. *MGMT* EX5-25C>T (rs12917) was associated with biliary tract cancer. Independent of gallstones, subjects carrying the CT genotype had a significantly reduced risk of gallbladder cancer (odds ratio [OR] = 0.63) and nonsignificantly reduced risks of bile duct (OR = 0.61) and ampulla of Vater (OR = 0.85) cancers. This marker was not associated with biliary stones. Findings suggest that *MGMT* gene variants may alter susceptibility to biliary tract cancer, particularly gallbladder cancer. **(Zhang M, Huang WY, Andreotti G, Gao YT, Rashid A, Chen J, Sakoda LC, Shen MC, Wang BS, Chanock S, Hsing AW. Variants of DNA repair genes and the risk of biliary tract cancers and stones: A population-based study in China. *Cancer Epidemiol Biomarkers Prev* 2008;17:2123–2127)**

Hepatitis B and C Virus Infection

Also in the Shanghai study, the authors examined the relationships of hepatitis B and C virus infection with risks of biliary tract cancer and biliary stones. Hepatitis B surface antigen (HBsAg) seroprevalence was 7.3% among controls and 14.2% among patients with extrahepatic bile duct cancer, resulting in a 2.4-fold risk. No association with HBsAg was found for cancers of the gallbladder or ampulla of Vater or for stones in the gallbladder or bile duct. Prevalence of hepatitis C infection in this population was low (2%), limiting the ability to detect an association with biliary diseases. **(Hsing AW, Zhang M, Rashid A, McGlynn KA, Wang BS, Niwa S, Ortiz-Conde BA, Goedert JJ, Fraumeni JF Jr, O'Brien TR, Gao YT. Hepatitis B and C virus infection and the risk of biliary tract cancer: A population-based study in China. *Int J Cancer* 2008;122:1849–1853)**

BLADDER CANCER

Urination Frequency

The effect of urination frequency on bladder cancer risk was evaluated in a large, multicenter case-control study, based on interviews conducted with 884 bladder cancer patients and 996 controls in Spain. A consistent, inverse trend in risk with increasing nighttime voiding frequency was observed in both men ($p = 0.0003$) and women ($p = 0.07$); voiding at least two times per night was associated with a significant, 40% to 50% risk reduction. The protective effect of nocturia was apparent among study participants with low, moderate, and high water consumption. The risk associated with cigarette smoking was reduced by nocturia. Compared with nonsmokers who did not urinate at night, current smokers who did not urinate at night had an OR of 7.0, whereas those who voided at least twice per night had an OR of 3.3 (p for trend = 0.0005). Findings suggest a strong protective effect of nocturia on bladder cancer risk, providing evidence that bladder cancer risk is related to the contact time of the urothelium with carcinogens in urine. Increased urination frequency, coupled with possible dilution of the urine from increased water intake, may diminish the effect of urinary carcinogens on bladder cancer risk. **(Silverman DT, Alguacil J, Rothman N, Real FX, García-Closas M, Cantor KP, Malats N, Tardón A, Serra C, García-Closas R, Carrato A, Lloreta J, Samanic C, Dosemeci M, Kogevinas M. Does increased urination frequency protect against bladder cancer? *Int J Cancer* 2008;123:1644–1648)**

BREAST CANCER

Use of SNPs for Risk Prediction

One purpose for seeking common alleles associated with disease is to use them to improve models for projecting individualized disease risk. Two genome-wide association studies (GWAS) and a study of candidate genes recently identified seven common SNPs, located in *FGFR2, TNRC9 (TOX3),*

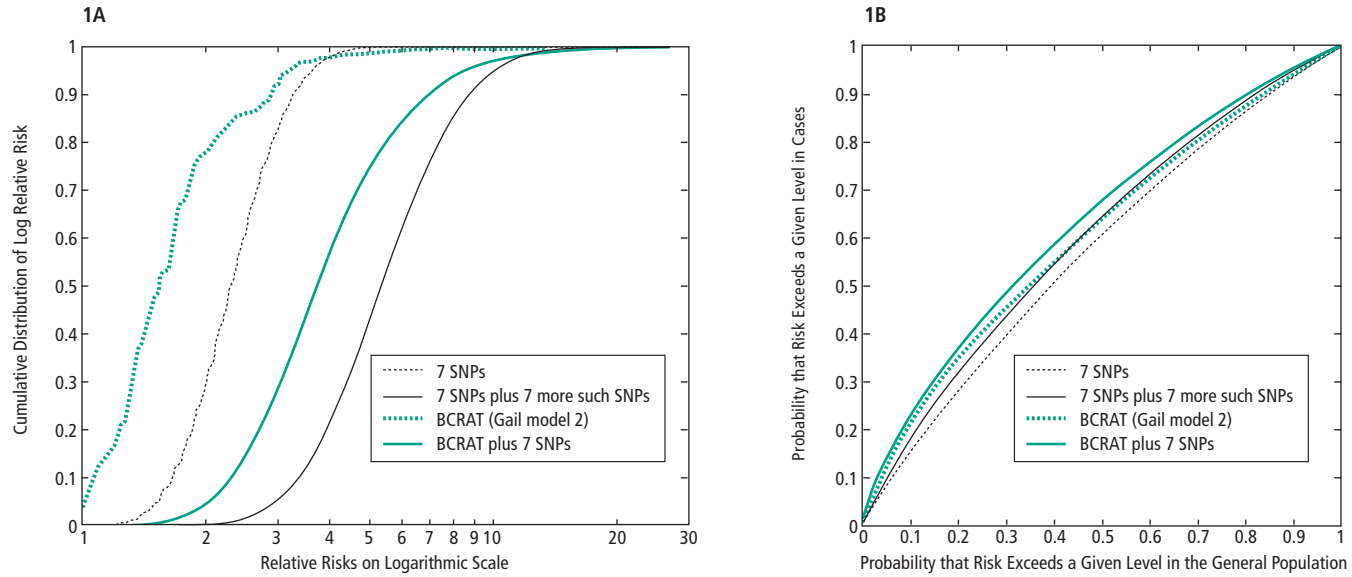


Figure 1. The cumulative distributions of log relative risk are shown for the 7 SNPs alone, for 14 such SNPs, for NCI's Breast Cancer Risk Assessment Tool (BCRAT), and for BCRAT plus the 7 SNPs (Figure 1A). Shallower slopes correspond to higher discriminatory accuracy. Another measure of discriminatory accuracy is the area under the curves in Figure 1B. (Gail MH, et al. 2008)

MAP3K1, LSP1, CASP8, chromosomal region 8q, and chromosomal region 2q35, that were associated with breast cancer risk in independent samples. Estimates of relative risks and allele frequencies from these studies were used to estimate how much these SNPs could improve discriminatory accuracy, measured as the area under the receiver operating characteristic curve (AUC). A model with these 7 SNPs (AUC = 0.574) and a hypothetical model with 14 such SNPs (AUC = 0.604) have less discriminatory accuracy than an existing model, NCI's Breast Cancer Risk Assessment Tool (BCRAT), which uses age at menarche and first live birth, family history of breast cancer, and history of breast biopsy examinations (AUC = 0.607). Adding the seven SNPs to BCRAT improved discriminatory accuracy to an AUC of 0.632, which was less than the improvement from adding mammographic density. Experience to date and quantitative arguments indicate that a huge increase in the numbers of subjects in GWAS would be required to find enough SNPs to achieve high discriminatory accuracy (see Figure 1). **(Gail MH. Discriminatory accuracy from single-nucleotide polymorphisms in models to predict breast cancer risk. *J Natl Cancer Inst* 2008;100:1037–1041)**

POWER CALCULATOR FOR GENETIC ASSOCIATION STUDIES

Statistical power calculations inform the design and interpretation of genetic association studies, but few programs are tailored to case-control studies of single nucleotide polymorphisms (SNPs) in unrelated subjects. The authors developed the "Power for Genetic Association analyses" (PGA) package, which comprises algorithms and graphical user interfaces for sample size and minimum detectable risk calculations using SNP or haplotype effects under different genetic models and study constraints. The software accounts for linkage disequilibrium and statistical multiple comparisons. The results are presented in graphs or tables and can be printed or exported in standard file formats. PGA is user-friendly software that can facilitate decision making for association studies of candidate genes, fine-mapping studies, and whole-genome scans. Stand-alone executable files and a Matlab toolbox are available for download at http://dceg.cancer.gov/bb/tools/pga. **(Menashe I, Rosenberg PS, Chen BE. PGA: Power calculator for case-control genetic association analyses. *BMC Genet* 2008;9:36)**

Genetic Variants Associated with Subtypes

The authors investigated whether associations between GWAS-identified SNPs in five loci (*FGFR2, TNRC9, MAP3K1,* 8q24, and *LSP1*) and breast cancer risk varied by clinically important tumor characteristics in up to 23,039 invasive breast cancer cases and 26,273 controls from 20 studies. Whether the SNPs influenced overall survival in 13,527

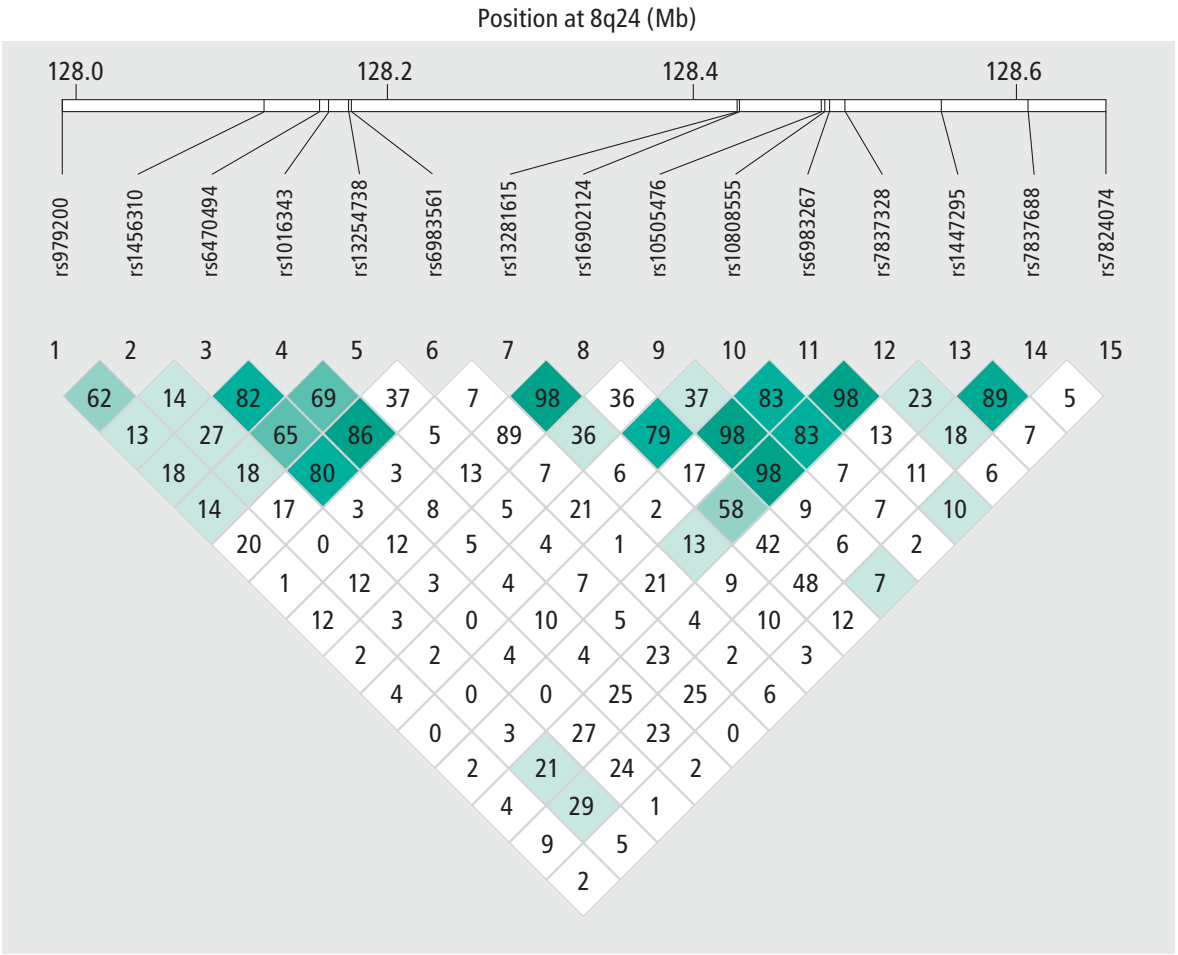


Figure 2. Pairwise linkage disequilibrium (*D'*) among the genotyped 8q24 polymorphisms in white controls from four studies. Diamond boxes represent the pairwise *D'* estimates between polymorphisms. (Berndt SI, et al. 2008)

cases from 13 studies was also assessed. rs2981582 in *FGFR2* was more strongly related to estrogen receptor (ER)-positive (OR [per allele] = 1.31) than ER-negative (OR [per allele] = 1.08) disease (p for heterogeneity = 10^{-13}). This SNP was also more strongly related to PR-positive, low-grade, and node-positive tumors ($p = 10^{-5}$, 10^{-8}, and 0.013, respectively). The association for rs13281615 in 8q24 was stronger for ER-positive, PR-positive, and low-grade tumors (p = 0.001, 0.011, and 10^{-4}, respectively). The differences in the associations between SNPs in *FGFR2* and 8q24 and risk by ER and grade remained significant after permutation adjustment for multiple comparisons and after adjustment for other tumor characteristics. Three SNPs (rs2981582, rs3803662, and rs889312) showed weak but significant associations with ER-negative disease; the strongest association was for rs3803662 in *TNRC9* (OR [per allele] = 1.14). rs13281615 in 8q24 was associated with an improvement in survival after diagnosis (hazard ratio [HR] [per allele] = 0.90), which was attenuated and nonsignificant after adjusting for known prognostic factors. Thus, common genetic variants differentially influence subtype-specific risks of breast cancer. Findings support the hypothesis that ER-positive and -negative disease are biologically distinct. **(García-Closas M, et al., for the Breast Cancer Association Consortium. Heterogeneity of breast cancer associations with five susceptibility loci by clinical and pathological characteristics. *PLoS Genet* 2008;4:e1000054)**

COLORECTAL CANCER

Risks Associated with Chromosome 8q24 Variants

The associations of 15 polymorphisms in chromosome 8q24 regions with risk were investigated in a pooled analysis of 2,587 colorectal adenoma cases, 547 colorectal cancer cases, and 2,798 controls from four studies. Three polymorphisms (rs10808555, rs6983267, and rs7837328) were found to be associated with colorectal tumor risk (see Figure 2). The association was strongest for the rs6983267 variant and was similar for adenoma (OR [per allele] = 1.16; p = 0.0002) and cancer (OR [per allele] = 1.17; p = 0.03). The strength of the association of the regional haplotype containing variant alleles at rs10808555,

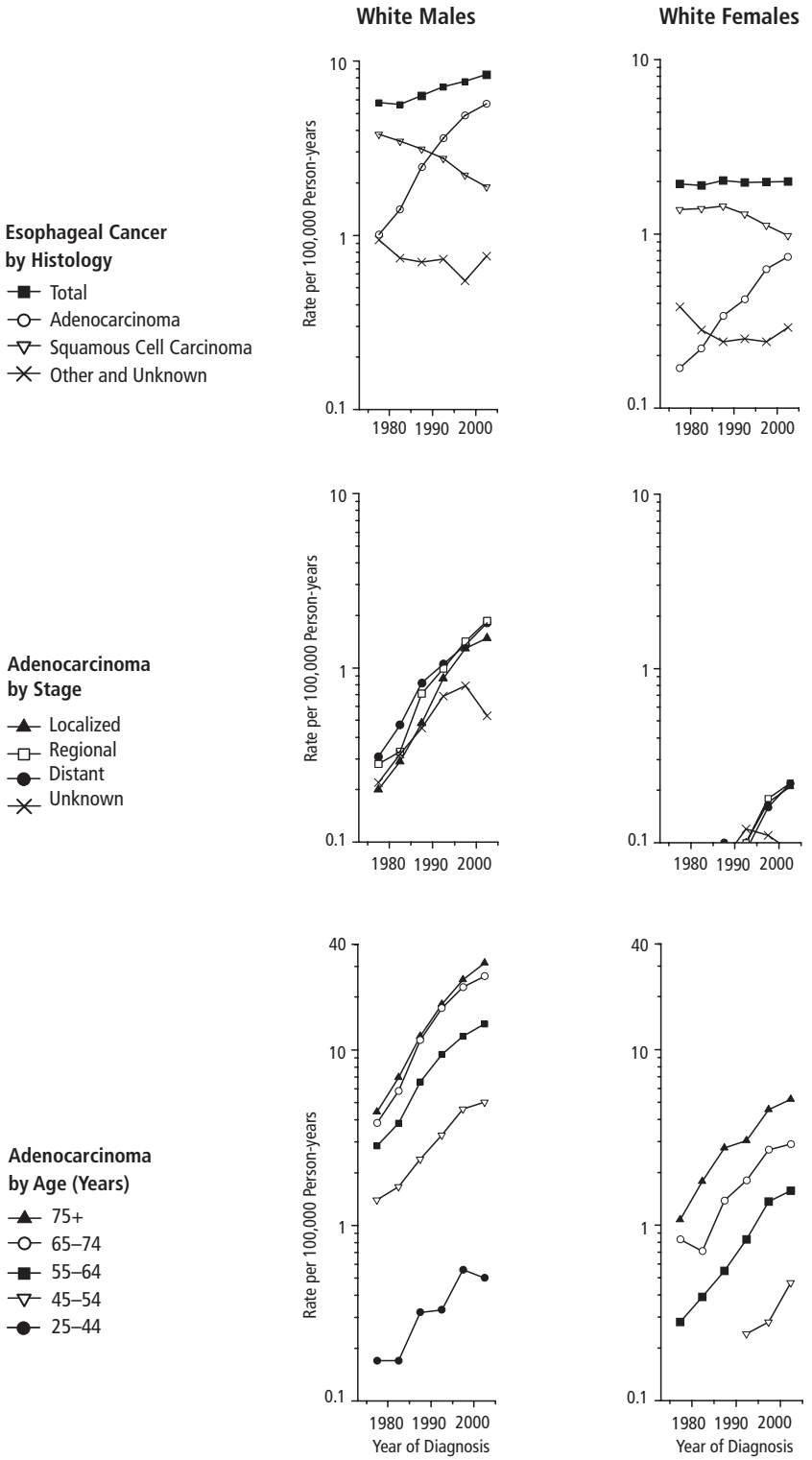


Figure 3. Trends in age-adjusted (2000 U.S. standard) esophageal cancer rates across five-year periods, from 1975 to 1979 through 2000 to 2004, among white individuals by sex. Data are from nine Surveillance, Epidemiology, and End Results registries. (Brown LM, et al. 2008)

rs6983267, and rs7837328 but not rs10505476 was greater than that of any single variant for adenoma (OR = 1.27; $p = 0.0001$) and cancer (OR = 1.26; $p = 0.03$). The risk associated with rs6983267 was stronger for multiple adenomas (OR [per allele] = 1.29; $p = 5.6 \times 10^{-6}$) than for single adenomas (OR [per allele] = 1.10; $p = 0.03$; (p for heterogeneity = 0.008). **(Berndt SI, Potter JD, Hazra A, Yeager M, Thomas G, Makar KW, Welch R, Cross AJ, Huang WY, Schoen RE, Giovannucci E, Chan AT, Chanock SJ, Peters U, Hunter DJ, Hayes RB. Pooled analysis of genetic variation at chromosome 8q24 and colorectal neoplasia risk. *Hum Mol Genet* 2008;17:2665–2672)**

ESOPHAGEAL CANCER

Continued Increases in Adenocarcinoma Incidence

Rapid increases in the incidence of adenocarcinoma of the esophagus have been reported among white men. Temporal patterns of this disease by sex, stage, and age were further explored using data from the Surveillance, Epidemiology, and End Results program. A total of 22,759 patients were diagnosed with esophageal cancer between 1975 and 2004, including 9,526 diagnosed with adenocarcinoma. Among white men, increases in the incidence of esophageal cancer were largely attributed to a 463% increase in the incidence of adenocarcinoma over this time period, from 1.01 per 100,000 person-years in 1975 to 1979 to 5.69 in 2000 to 2004. A similar rapid increase was also apparent among white women, among whom the adenocarcinoma rate increased 335%, from 0.17 to 0.74 per 100,000 person-years, over the same time period. Adenocarcinoma rates rose among white men and women in all stage and age groups (see Figure 3). **(Brown LM, Devesa SS, Chow WH. Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. *J Natl Cancer Inst* 2008;100:1184–1187)**

HIV-RELATED CANCERS

Cancer Risk in HIV-infected Persons

The authors linked HIV/AIDS and cancer registries in three states to study cancer risk among 57,350 HIV-infected persons (initially AIDS-free) registered between 1991 and 2002. Subjects were followed for five years after registration, and 871 cancers occurred. Risk was elevated for Kaposi sarcoma (KS, standardized incidence ratio [SIR] = 1,300), non-Hodgkin lymphoma (NHL, SIR = 7.3), cervical cancer (SIR = 2.9), and several non–AIDS-defining malignancies, including Hodgkin lymphoma (SIR = 5.6) and cancers of the lung (SIR = 2.6) and liver (SIR = 2.7). KS and NHL incidence declined over time but remained elevated in 1996 to 2002. Incidence increased in 1996 to 2002 compared with 1991 to 1995 for Hodgkin lymphoma (relative risk [RR] = 2.7) and liver cancer (RR = infinite). Non–AIDS-defining cancers comprised 31.4% of cancers in 1991 to 1995 vs. 58.0% in 1996 to 2002. For KS and NHL, risk was inversely related to CD4 count, but these associations attenuated after 1996. Thus, KS and NHL incidence declined markedly in recent years, likely reflecting highly active antiretroviral therapy (HAART)-related improvements in immunity, whereas incidence of some non–AIDS-defining cancers increased, resulting in a shift in the spectrum of cancer among HIV-infected persons. **(Engels EA, Biggar RJ, Hall HI, Cross H, Crutchfield A, Finch JL, Grigg R, Hylton T, Pawlish KS, McNeel TS, Goedert JJ. Cancer risk in people infected with human immunodeficiency virus in the United States. *Int J Cancer* 2008;123:187–194)**

Conjunctival Squamous Cell Carcinoma in Persons with AIDS

Squamous cell carcinoma of the conjunctiva (SCCC) has been associated with HIV infection in equatorial Africa. The authors assessed the risk for SCCC and other eye cancers in the updated U.S. HIV/AIDS Cancer Match Study. Based on a study of 491,048 adults with AIDS, SIRs were elevated for SCCC (n = 15; SIR = 12.2), primary ocular lymphoma (n = 35; SIR = 21.7), and ocular KS (n = 17; SIR = 109). Risk for SCCC was elevated regardless of HIV acquisition category, CD4 lymphocyte count, or time relative to AIDS onset. The proportions of eye cancers that were SCCC were highest with greater age, Hispanic ethnicity, and residence in regions with high solar ultraviolet radiation. **(Guech-Ongey M, Engels EA, Goedert JJ, Biggar RJ, Mbulaiteye SM. Elevated risk for squamous cell carcinoma of the conjunctiva among adults with AIDS in the United States. *Int J Cancer* 2008;122:2590–2593)**

KIDNEY CANCER

Role of Body Size and Physical Activity

The relationship between body mass index (BMI) and invasive renal cell carcinoma (RCC) was analyzed in the NIH-AARP Diet and Health Study, a large, prospective cohort of participants aged 50 to 71 years at baseline in 1995 to 1996, with follow-up through 2003. Detailed analyses were conducted in a subcohort assessing BMI at younger ages (18, 35, and 50 years), weight change across three consecutive age intervals, waist and hip size as well as waist-to-hip ratio, and height at age 18. Among 1,022 male and 344 female cases, RCC was strongly related to BMI at study baseline. Among subjects analyzed in the subcohort, RCC associations were strongest for baseline BMI and recalled BMI at age 50 and were successively attenuated for recalled BMI at ages 35 and 18. Weight gain in early (18–35 years of age) and mid-adulthood (35–50 years of age) was strongly associated with RCC, whereas weight gain after midlife (age 50 years to baseline) was unrelated. RCC was positively associated with waist-to-hip ratio in women and with height at age 18 in men and women. **(Adams KF, Leitzmann MF, Albanes D, Kipnis V, Moore SC, Schatzkin A, Chow WH. Body size and renal cell cancer incidence in a large US cohort study. *Am J Epidemiol* 2008;168:268–277)**

In a related study, the authors examined physical activity in relation to renal cell carcinoma among 482,386 participants who reported their frequency of exercise of at least 20 minutes' duration, intensity of daily activity, and frequency of physical activity during adolescence. During follow-up, 1,238 cases of renal cell cancer were ascertained. Current exercise, routine physical activity, and activity during adolescence were associated with reduced risk. **(Moore SC, Chow WH, Schatzkin A, Adams KF, Park Y, Ballard-Barbash R, Hollenbeck A, Leitzmann MF. Physical activity during adulthood and adolescence in relation to renal cell cancer. *Am J Epidemiol* 2008;168:149–157)**

LUNG CANCER

Pathway-based Candidate Gene Evaluation

A pathway-based candidate gene evaluation was conducted to identify genetic variations that may be associated with lung cancer in a population-based case-control study in Xuan Wei, China (122 cases and 111 controls). A total of 1,260 SNPs in 380 candidate genes for lung cancer were successfully genotyped and assigned to 1 of 10 pathways based on gene ontology. The cell cycle pathway was found to be the most important pathway, with four genes significantly associated with lung cancer, after adjusting for multiple comparisons. Most cell cycle genes that were associated with lung cancer in this analysis were concentrated in the AKT signaling pathway, which is essential for regulation of cell cycle progression and cellular survival and may be important in lung cancer etiology in Xuan Wei.

(Hosgood HD III, Menashe I, Shen M, Yeager M, Yuenger J, Rajaraman P, He X, Chatterjee N, Caporaso N, Zhu Y, Chanock S, Zheng T, Lan Q. Pathway-based evaluation of 380 candidate genes and lung cancer susceptibility suggests the importance of the cell cycle pathway. *Carcinogenesis* 2008;29:1938–1943)

Gender, Smoking, and Lung Cancer Risk

To address whether women are more susceptible than men to lung cancer caused by cigarette smoking, incidence rates of lung cancer by strata of smoking use were compared in men and women in the NIH-AARP cohort. A total of 279,214 men and 184,623 women aged 50 to 71 years at study baseline were included in this analysis, with lung cancers occurring among 4,097 men and 2,237 women. Incidence rates were 20.3 per 100,000 person-years in men who had never smoked (99 cancers) and 25.3 in women who had never smoked (152 cancers; HR = 1.3 for women compared with men). The incidence rate among current smokers who smoked more than two packs per day was 1,259.2 in men and 1,308.9 in women. In current smokers, in a model adjusted for typical smoking dose, the HR was 0.9 for women compared with men. In former smokers, in a model adjusted for years of cessation and typical smoking dose, the HR was 0.9 for women compared with men. Incidence rates of adenocarcinoma, small-cell carcinoma, and undifferentiated tumors were similar in men and women, but rates of squamous tumors in men were somewhat higher than those in women. Findings suggest that women are not more susceptible than men to the carcinogenic effects of cigarette smoking in the lung. In smokers, incidence rates tended to be higher in men than women with comparable smoking histories, but differences were modest. (Freedman ND, Leitzmann MF, Hollenbeck AR, Schatzkin A, Abnet CC. Cigarette smoking and subsequent risk of lung cancer in men and women: Analysis of a prospective cohort study. *Lancet Oncol* 2008;9:649–656)

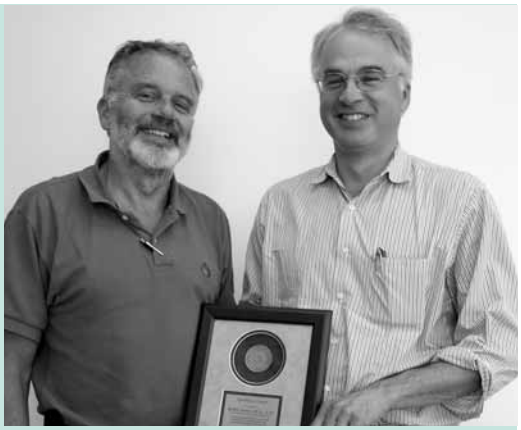
DCEG STAFF WIN NIH DIRECTOR'S AWARDS

In July, several DCEG staff members were recognized at the annual NIH Director's Awards Ceremony for their superior performance. NIH Director Elias A. Zerhouni, M.D., who stepped down in October, presented awards to the following staff members:

The Genome-wide Association Studies (GWAS) Policy Development Team members: **Stephen J. Chanock, M.D.,** Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, and **Robert N. Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, along with staff members from other NIH institutes, for their teamwork, skill, and dedication in the development of the landmark NIH GWAS data-sharing policy.

Shelia Hoar Zahm, Sc.D., DCEG Deputy Director, along with Elaine J. Ayres and Dr. John I. Gallin (both of the NIH Clinical Center), for their leadership of a committee to evaluate biospecimen storage and tracking in the NIH Intramural Research Program.

In addition, **Demetrius Albanes, M.D.,** Nutritional Epidemiology Branch, received a U.S. Public Health Service Outstanding Service Medal for his research contributions on micronutrient effects in cancer.



Robert Hoover and Stephen Chanock

John Gallin, Shelia Zahm, and Elaine Ayres.

Demetrius Albanes

LYMPHOMA

Lymphoproliferative Disorders in Relatives

To quantify relative risks of lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (LPL/WM) and other lymphoproliferative disorders in first-degree relatives of LPL/WM patients, the authors identified 2,144 LPL/WM patients (1,539 WM and 605 LPL) diagnosed in Sweden, 8,279 population-based matched controls, and linkable first-degree relatives of patients (n = 6,177) and controls (n = 24,609). First-degree relatives of LPL/WM patients were found to have 20-fold, 3-fold, 3.4-fold, and 5-fold increased risks of LPL/WM, NHL, chronic lymphocytic leukemia (CLL), and monoclonal gammopathy of undetermined significance (MGUS), respectively, whereas there was no evidence of an increased risk of

developing multiple myeloma or Hodgkin lymphoma. In analyses stratified by type of first-degree relative (parent, sibling, or offspring), age at diagnosis of the probands (above or below 70 years), and sex of the first-degree relative, the risk estimates were not significantly different from the overall analyses. Findings of highly increased risks of developing LPL/WM, NHL, CLL, and MGUS support the operation of shared susceptibility genes that predispose to LPL/WM and other lymphoproliferative disorders. **(Kristinsson SY, Björkholm M, Goldin LR, McMaster ML, Turesson I, Landgren O. Risk of lymphoproliferative disorders among first-degree relatives of lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia patients: A population-based study in Sweden. *Blood* 2008;112:3052–3056)**

MYELOPROLIFERATIVE NEOPLASMS

Risks in First-degree Relatives

Previous small studies have reported familial clustering of myeloproliferative neoplasms (MPNs), including polycythemia vera (PV), essential thrombocythemia (ET), and myelofibrosis (MF). To quantify risks of various types of MPNs and related malignancies among relatives, the authors identified 6,217 PV, 2,838 ET, 1,172 MF, and 812 MPN not otherwise specified (NOS) patients diagnosed in Sweden; 43,550 controls; and first-degree relatives of cases (n = 24,577) and controls (n = 99,542). Relatives of MPN patients had significantly increased risks of PV (relative risk [RR] = 5.7), ET (RR = 7.4), and MPN NOS (RR = 7.5). Analyses stratified by type of first-degree relative revealed consistently higher risks for siblings compatible with a model of recessive genetic inheritance. Mean age at MPN diagnosis was not different for affected relatives of cases (57.5 years) vs. controls (60.6 years), and risk of MPN by age was not different for parents vs. offspring of MPN cases. Relatives of MPN patients also had a borderline increased risk of chronic myeloid leukemia (RR = 1.9; p = 0.09). Findings among first-degree relatives of MPN patients support the hypothesis that there are common, strong, shared susceptibility genes. **(Landgren O, Goldin LR, Kristinsson SY, Helgadottir EA, Samuelsson J, Björkholm M. Increased risks of polycythemia vera, essential thrombocythemia, and myelofibrosis among 24,577 first-degree relatives of 11,039 patients with myeloproliferative neoplasms in Sweden. *Blood* 2008;112:2199–2204)**

PROSTATE CANCER

Risk Associated with Serum Vitamin D Levels

The association between serum 25-hydroxyvitamin D (25[OH]D) level and risk of prostate cancer was investigated in a case-control study nested within the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. The study included 749 patients with incident prostate cancer diagnosed one to eight years after blood draw and 781 matched controls. All study participants were selected from the trial screening arm, which included annual standardized prostate cancer screening. No significant trend in overall prostate cancer risk was observed with increasing season-standardized serum 25(OH)D level. However, serum 25(OH)D concentrations greater than the lowest quintile (Q1) were associated with increased risk of aggressive (Gleason sum $\geq$ 7 or clinical stage III or IV) disease (in a model adjusting for matching factors, study center, and history of diabetes, ORs for Q2 vs. Q1 = 1.20, for Q3 vs. Q1 =1.96, for Q4 vs. Q1 = 1.61, and for Q5 vs. Q1 = 1.37; p for trend = 0.05). The rates of aggressive prostate cancer for increasing quintiles of serum 25(OH)D were 406, 479, 780, 633, and 544 per 100,000 person-years. In exploratory analyses, these associations with aggressive disease were consistent across subgroups defined by age, family history of prostate cancer, diabetes, BMI, vigorous physical activity, calcium intake, study center, season of blood collection, and assay batch. The findings of this large prospective study do not support the hypothesis that vitamin D is associated with decreased risk of prostate cancer; indeed, higher circulating 25(OH)D concentrations may be associated with increased risk of aggressive disease. **(Ahn J, Peters U, Albanes D, Purdue MP, Abnet CC, Chatterjee N, Horst RL, Hollis BW, Huang WY, Shikany JM, Hayes RB; Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Project Team. Serum vitamin D concentration and prostate cancer risk: A nested case-control study. *J Natl Cancer Inst* 2008:100:796–804)**

TESTICULAR CANCER

Insulin-like Growth Factor and Binding Protein Levels

The authors examined associations between testicular germ-cell tumor risk and circulating concentrations of insulin-like growth factor 1 (IGF-1) and insulin-like growth factor–binding protein 3 (IGFBP-3) among 517 cases and 790 controls from the U.S. Servicemen's Testicular Tumor Environmental and Endocrine Determinants (STEED) Study. Overall, there were no associations between IGF-1 or IGFBP-3 concentrations and risk of testicular germ-cell tumors; however, when cases were separated by histologic type, there was a suggestion of a reduction in seminoma risk associated with the highest concentrations of IGF-1 compared with the lowest concentrations (OR = 0.66), contrary to expectation. **(Chia VM, Quraishi SM, Graubard BI, Rubertone MV, Erickson RL, Stanczyk FZ, McGlynn KA. Insulin-like growth factor 1, insulin-like growth factor–binding protein 3, and testicular germ-cell tumor risk. *Am J Epidemiol* 2008;167:1438–1445)**

DCEG PEOPLE IN THE NEWS

In June, **Amy Berrington de Gonzalez, D.Phil., Parveen Bhatti, Ph.D., Andre Bouville, Ph.D., Alina V. Brenner, M.D., Ph.D.,** and **Alice J. Sigurdson, Ph.D.,** all of the Radiation Epidemiology Branch (REB), gave invited lectures at the 2008 American Statistical Association Conference on Radiation and Health in Vail, Colorado. Dr. Berrington de Gonzalez discussed "Cancer risks related to CT scan use in the U.S."; Dr. Bhatti spoke on "Fluorescence *in situ* hybridization and diagnostic radiation exposure in radiologic technologists"; Dr. Bouville talked about "Using biodosimetry to estimate doses in retrospective studies"; Dr. Brenner spoke on "Lung cancer in fluoroscopy patients: Massachusetts cohort"; and Dr. Sigurdson lectured on the "Risk of cataract attributable to personal diagnostic radiation exposure among radiation technologists."

In July, **Louise A. Brinton, Ph.D.,** Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), gave a talk on "Cancer risks after fertility treatment in females" at the 24th Annual Meeting of the European Society of Human Reproduction and Embryology in Barcelona. Dr. Brinton also gave a talk on "Prospective evaluation of risk factors for male breast cancer" at the 41st Annual Meeting of the Society for Epidemiologic Research in Chicago in June. At the same meeting, **Kim N. Danforth, Sc.D.** (HREB), spoke on "Postmenopausal hormone use and ovarian cancer risk: An update of the NIH-AARP Diet and Health Study"; **Gretchen L. Gierach, Ph.D., M.P.H.** (HREB), presented a poster on "Physical activity and endometrial cancer risk in the NIH-AARP Diet and Health Study"; Dr. Gierach and **Maureen C. Hatch, Ph.D.** (REB), cochaired a Spotlight Session on "Current topics in breast cancer research"; and **Cari Meinhold, M.H.S.,** Nutritional Epidemiology Branch (NEB), gave a talk on "Predictors of insulin and glucose and the risk of pancreatic cancer in smokers."

This summer, **Eric A. Engels, M.D., M.P.H.,** Infections and Immunoepidemiology Branch (IIB), gave several talks: "Transplant Cancer Match Study" at the Secretary of Health and Human Services Advisory Committee on Organ Transplantation in Rockville; "Infections as causes of non-Hodgkin lymphoma: An overview" at a Stockholm meeting titled Leukemia and Lymphoma Development—The Role of Inflammation, Autoimmunity, and Infections; "New insights into the epidemiology and outcome of lung cancer in HIV-infected patients" at the American Thoracic Society Meeting in Toronto; and "Research priorities in epidemiology: Non–AIDS-defining cancers" at the AIDS Malignancy Working Group meeting at NCI in Bethesda.

In August, **Mitchell H. Gail, M.D., Ph.D.,** Biostatistics Branch (BB), gave an invited session at the Joint Statistical Meetings in Denver on "Probability of detecting disease-associated SNPs in case-control genome-wide association studies." At the same meeting, **Hormuzd A. Katki, Ph.D.** (BB), gave an invited presentation on "Estimating family relationships using DNA fingerprints in the NHANES-III Household Survey."

In May, **Montserrat García-Closas, M.D., Dr.P.H.** (HREB), gave an NIH Director's Seminar Series lecture on "Advances in the understanding of genetic susceptibility to breast cancer."

In May, **Lynn R. Goldin, Ph.D.,** Genetic Epidemiology Branch (GEB), spoke on "Finding cancer susceptibility genes: Family and population approaches" at the Columbia University Genetic Epidemiology Seminar.

In September, Dr. Hatch gave an invited talk on "Thyroid cancer among those exposed *in utero* or as children to I-131 from Chornobyl fallout" at the Thyroid Cancer State of Science conference, Chornobyl and Beyond, held in Bethesda.

Farin Kamangar, M.D., Ph.D. (NEB), gave a talk on "Investigating the etiology of esophageal cancer in a high-risk area of Iran: Old and new risk factors" at the Fred Hutchinson Cancer Research Center in Seattle in May and at the Johns Hopkins Bloomberg School of Public Health in Baltimore in June.

In April, Dr. Katki gave a presentation on "The close relationship between false discovery rates and statistical evidence as quantified by Bayes factors" at the Department of Mathematics and Statistics, University of Maryland, Baltimore County.

In April, **Maria Teresa Landi, M.D., Ph.D.** (GEB), gave a presentation on "Integration of data from germline and somatic changes in the etiology of cancer" at the NIH Clinical Center. Later in the month, she spoke on "Genetic susceptibility in melanoma etiology" at Yale Cancer Center Grand Rounds and on "An integrative approach to look at lung cancer etiology" at the Department of Genetics Seminar at Yale University School of Medicine. In May, she served as cochair of the Clinical Epidemiology of Melanoma Session of the International Pigment Cell Conference and the International Melanoma Research Congress held at the Sapporo Medical University in Japan, and she gave an invited talk on the "Role of

heredity, the environment, and somatic changes in melanoma treatment and clinical outcome."

In July, **Martha S. Linet, M.D., M.P.H.,** Chief of REB, gave two presentations: "A feasibility study to improve questionnaire-based sun exposure measures for epidemiologic studies of cancer" at the Queensland University of Technology in Brisbane, Australia and "Diagnostic medical radiation and risk of childhood cancer" at the Murdoch Childrens Research Institute at the Royal Children's Hospital in Melbourne. In September, she gave a talk on "Government: Combining research and service work" at a career forum at the American College of Epidemiology meeting in Tucson.

Jennifer T. Loud, R.N., C.R.N.P., D.N.P., Clinical Genetics Branch (CGB), has been appointed Assistant Branch Chief of CGB. She is a lead investigator on a breast imaging protocol, has helped develop the Branch's behavioral and psychosocial research studies, and is a national leader in the Oncology Nursing Society's Cancer Genetics and Nurse Practitioner special interest groups. In May, she presented a talk on "The use of family history in screening for individuals at risk of cancer" at the Oncology Nursing Society meeting in Philadelphia, and in June, she gave a talk on genetics and genomics at the Georgetown University School of Nursing and Health Studies.

In June, Dr. Gierach and **Gwen Murphy, Ph.D., M.P.H.** (IIB), received NCI Merit Awards in Cancer Prevention Research Training. The awards recognize outstanding performance as Cancer Prevention Fellows.

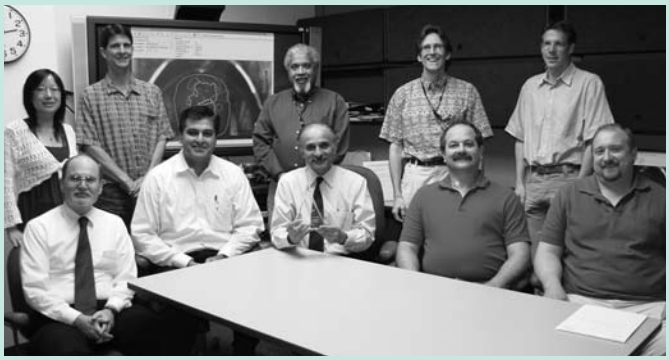
In May, **Thomas R. O'Brien, M.D., M.P.H.,** Epidemiology and Biostatistics Program, presented findings on "Variants in interferon-α pathway genes and response to treatment of chronic hepatitis C" at the Digestive Disease Week conference in San Diego. He was recently named an Associate Editor of the *American Journal of Epidemiology.*

In April, **Charles S. Rabkin, M.D.** (IIB), chaired an American Association for Cancer Research Educational Session on "Chronic infection and carcinogenesis: Biology and application" held in San Diego. He also gave invited talks on "Molecular epidemiology of infection-related malignancy" at the Refractory Diseases Caused by Viral Infection Symposium at the Kagoshima University Graduate School of Medical and Dental Sciences in Japan in March and at the University of Iowa Holden Comprehensive Cancer Center in May.

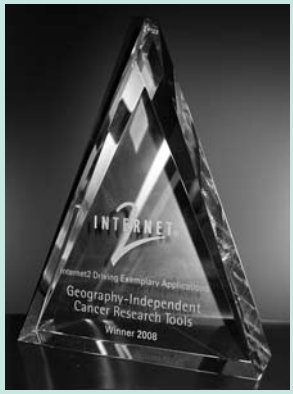
A number of DCEG fellows and investigators were actively involved in planning and hosting the NCI Summer Curriculum in Cancer Prevention. Dr. Gierach hosted the hormonal and reproductive sessions of the Epidemiology, Prevention, and Control of Site-Specific Tumors module; Dr. Murphy hosted the Disseminating Scientific Knowledge module; and **Joanne L. Watters, Ph.D., M.P.H.** (NEB), hosted the Diet and Cancer Prevention module. **Dana M. Van Bemmel, Ph.D., M.P.H.,** Occupational and Environmental Epidemiology Branch, was involved in planning the Molecular Prevention component of the course. In addition, **Arthur Schatzkin, M.D., Dr.P.H.,** Chief of NEB, gave a talk on "Diet in cancer at a crossroads: Do we know what to believe—or even believe what we know?" and **Amanda J. Cross, Ph.D.** (NEB), spoke on "Colorectal cancer."

INTERNET2 IDEA AWARD

In April, **Mark Schiffman, M.D., M.P.H.** (HREB), along with Dr. Sameer Antani, Rodney Long, and Dr. George Thoma of the National Library of Medicine, received an Internet2 IDEA award for developing network-based tools and techniques that use the speed and capability of research networks such as Internet2. These resources enable doctors from around the world to better participate in cancer research studies and conduct more comprehensive data analysis. The tools include systems to store thousands of images and patient records, providing access to images by shape, color, and texture features. The focus of the team's current research is cervical cancer and human papillomavirus. The DCEG component was led by Dr. Schiffman and Dr. Jose Jeronimo, formerly of HREB and now with PATH (Program for Appropriate Technology in Health). The award was presented at the spring 2008 Internet2 meeting in Arlington, Virginia.



Team Members: (front) Rodney Long, Sameer Antani, George Thoma, Mark Schiffman, and Scott Budihas; (back) Jaylene Xue, Leif Neve, Carl Cornwell, Mike Bopf, and Nicolas Wentzensen.



COMINGS . . . GOINGS


Samsiddhi Bhattacharjee

In September, **Samsiddhi Bhattacharjee, Ph.D.,** joined the Biostatistics Branch (BB) as a research fellow after receiving his doctorate in human genetics at the University of Pittsburgh. He also has a master's degree in statistics from the Indian Statistical Institute in Kolkata. Working with **Nilanjan Chatterjee, Ph.D.,** he will develop and apply statistical and computational tools for identifying genetic variants, networks, and pathways that affect susceptibility to human diseases.


Aileen Burke

Aileen Burke has joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a predoctoral Cancer Research Training Award (CRTA) fellow. She received her B.S. in pharmacology from the National University of Ireland in Dublin in 2004. She subsequently held laboratory positions at NCI, where she was involved with research on protein-DNA interactions and cell signaling pathways. She is currently completing her M.P.H. in epidemiology at George Washington University. Her training as a molecular biologist and experience in laboratory research involving hormone pathways in cancer make her a valuable addition to the team of investigators clarifying the etiology of female cancers.

After completing a 10-month sabbatical in HREB, **Maíre A. Duggan, M.D.,** has returned to her position as senior gynecologic pathologist and professor at the University of Calgary in Canada.


Kyoji Furukawa

As a special volunteer from the Radiation Effects Research Foundation (RERF) in Hiroshima, Japan, **Kyoji Furukawa, Ph.D.,** has joined the Radiation Epidemiology Branch (REB) for six months. He is an expert in biostatistics and has a special interest in developing Bayesian analytical methods applicable to radiation risk estimates in the RERF cohort studies of atomic bomb survivors in Hiroshima and Nagasaki. With mentoring from **Kiyohiko Mabuchi, M.D., Dr.P.H.,** he is studying radiation risk assessment in radiation-exposed cohorts.


Stephanie George

Stephanie George, M.P.H., M.A., has joined the Nutritional Epidemiology Branch (NEB) as a predoctoral fellow under the Yale University/NCI Partnership Training Program. She will be working with mentors **Demetrius Albanes, M.D.,** and Dr. Susan Mayne, from the Yale School of Public Health, to better explore the association between energy balance and breast cancer among breast cancer survivors and healthy individuals with a focus on evaluating specific aspects of diet, anthropometry, and physical activity.

After a two-year research fellowship in REB, **Kwang Pyo Kim, Ph.D.,** returned to Korea to take a position in the Department of Nuclear Engineering at Kyung Hee University in September. During his time in REB, Dr. Kim served as the dosimetrist for studies of cancer risk among medical personnel providing fluoroscopically guided procedures and among patients undergoing computed tomography scans.

Michael F. Leitzmann, M.D., Dr.P.H., left NEB to direct the Institute of Epidemiology and Preventive Medicine at the University of Regensburg in Germany.

In August, **Yan Li, Ph.D.,** left BB after two years as a research fellow to take a position as an assistant professor in the Department of Mathematics of the University of Texas at Arlington.

In June, **Sheng Luo, Ph.D.,** left BB after a two-year stay as a predoctoral/postdoctoral fellow to take a position as an

After a long career, including 32 years of federal service and 13 years in the private sector, **Nancy Carter** retired from the Epidemiology and Biostatistics Program (EBP) in June. She began her NIH career at the National Institute of Mental Health in the Child Psychiatry Branch and, after five years, moved to NCI, where she worked first in the former Environmental Epidemiology Branch. As the long-time secretary to **Robert N. Hoover, M.D., Sc.D.,** Director of EBP, she brought her professional administrative skills and cheerful personality to bear upon every situation. She was directly responsible for the administrative oversight of every aspect of the program, including personnel, budget, travel, site visits, and contracts. In addition, she coordinated the diethylstilbestrol study group, including its annual meetings and conferences.


Nancy Carter receives DCEG Special Appreciation Award from Joseph Fraumeni.

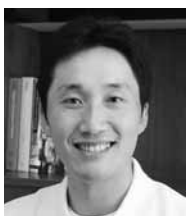
assistant professor in the Division of Biostatistics at the University of Texas School of Public Health in Houston.


Sandra Mora

In July, **Sandra Mora** joined the Infections and Immunoepidemiology Branch (IIB) as a program support assistant.

After a two-year visiting fellowship in REB, **Evgenia Ostroumova, Ph.D.,** has returned to the Epidemiology Laboratory at the Urals Research Center for Radiation Medicine in Chelyabinsk, Russia. She worked with **Martha S. Linet, M.D., M.P.H.** (REB), and **Susan S. Devesa, Ph.D.** (BB), on an analysis of international variation in incidence of childhood hematopoietic malignancies. She will continue to work on a study of cancer risks for adults and people exposed *in utero* in the Techa River population with **Elaine Ron, Ph.D.** (REB). She also worked on the Ukrainian-American Chornobyl Thyroid Study, analyzing the dose-response relationship between iodine-131 and prevalent mild hypothyroidism.

After a year as a visiting scientist in the Occupational and Environmental Epidemiology Branch (OEEB), **Dong-uk Park, Ph.D.,** has returned to the Department of Environmental Health in the Korea National Open University in Seoul. During his stay, he pursued his interest in research on occupational exposures to metalworking fluids, lead, and asbestos.


Ju-Hyun Park

In September, **Ju-Hyun Park, Ph.D.,** joined BB as a CRTA fellow after completing his doctorate in biostatistics at the University of North Carolina at Chapel Hill and a predoctoral fellowship at the National Institute of Environmental Health Sciences. He will be working with Dr. Chatterjee to develop Bayesian statistical approaches for flexible design and analysis of epidemiologic studies.

Cristina Poscablo, a predoctoral fellow in OEEB, has left to attend medical school at George Washington University. During her stay in OEEB, she assisted **Lee E. Moore, Ph.D.,** on molecular and epigenetic studies of bladder cancer conducted in Argentina, Spain, and New England.


Lisa Prokop

Lisa Prokop has joined the Office of Communications and Special Initiatives as an NCI Health Communications Intern. She is currently a student at the Johns Hopkins Bloomberg School of Public Health, where she is pursuing an M.H.S. with a concentration in health communication. She is working with **Alyssa Voss, M.P.H.,** and **Jennifer Loukissas, M.P.P.,** in responding to press and congressional inquiries, preparing DCEG investigators for interactions with the media, and translating scientific findings into practical and accessible public health messages.


Edgar Simard

Edgar Simard, M.P.H., has joined IIB as a predoctoral fellow. He received a B.S. in public health from Southern Connecticut State University and an M.P.H. from the Emory University Rollins School of Public Health. He previously worked as an epidemiologist at CDC. He is currently a Ph.D. candidate in the epidemiology program at the University of Medicine and Dentistry of New Jersey School of Public Health. For his dissertation research, he will be working with **Eric A. Engels, M.D., M.P.H.,** to examine cancer among persons with late-stage AIDS.

In August, **Dana M. Van Bemmel, Ph.D., M.P.H.,** left OEEB to join the NCI Center for Cancer Training as the Associate Director for the Cancer Prevention Fellowship Program. During her Cancer Prevention Fellowship in OEEB, she worked with Dr. Moore on molecular epidemiology studies of renal and bladder cancer, collaborated with various members of the Division, and worked on projects with investigators in the Division of Cancer Prevention and the Center for Cancer Research.

SHARON MILLER RETIRES


Sharon Miller

In May, **Sharon Miller** retired from the NCI Office of Acquisitions. During her 34-year career, she played an instrumental role in the field of contracting. She received multiple awards from NIH and other agencies during her career, including the NCI Director's Award, a DCEG Special Recognition Award, NCI Customer Service Awards in four consecutive years, Sustained Superior Performance Awards, and National Contract Management Association (NCMA) Special Recognition Awards. She also served as President and National Director of the Bethesda/Medical Chapter of NCMA. Her contributions were key to the successful conduct of the DCEG research program.

Ms. Miller began her career in the federal government in 1974 and joined NCI in 1981 as a contract administrator. In 1983, she accepted a contract specialist trainee position, where she flourished. She was promoted to contracting officer/team leader in 1988. In 1997, she became deputy chief of the Epidemiology and Support Section. Throughout her career, she took pride in being a true partner to her Project Officers and in assisting them to achieve their scientific goals. She plans to spend her retirement traveling, working on her historic home, and spending time with her children and grandchildren.

DCEG STAFF AT WORK AND PLAY

Annual Staff Picnic




DCEG staff gather for good food, fun, physical activity, and camaraderie at the annual picnic at Cabin John Park in Bethesda.

Time Management Workshop

Ann Hsing, the DCEG Women Scientist Advisor, sponsors a half-day Time Management Workshop for staff.

Fellows' Colloquium


Speakers Mary Ward, Patricia Hartge, and Sophia Wang discuss career development and scientific initiatives with fellows at the September colloquium.

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