National Cancer Institute

DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS

Linkage

MARCH 2009 • NUMBER 35

IN THIS ISSUE:

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Cohort Consortium Flourishing as It Enters Ninth Year

In November, more than 100 investigators from 12 countries gathered in Bethesda for the eighth annual meeting of the NCI Cohort Consortium. Created in 2000, this extramural/intramural consortium addresses critical areas of cancer etiology research in which large-scale collaborations with sufficient data and biospecimens are needed to study gene-gene and gene-environment interactions. DCEG and the Division of Cancer Control and Population Sciences (DCCPS) have initiated, fostered, and supported this important research collaborative.

The consortium has grown steadily since its inception, attracting new cohorts and new investigators. In 2008, the consortium was joined by the DCEG U.S. Radiologic Technologists Study; the Canadian Study of Diet, Lifestyle, and Health; and the Swedish Women's Lifestyle and Health Study. These new members bring the total number of cohorts to 37, representing about 4 million study subjects, with some cohorts still accruing participants.

Consortium research projects are tackling some of the most challenging questions in the cancer field, which have been difficult to answer with existing studies. The large number of study subjects in the consortium permits the detection of modest

Cohort Consortium Meeting Organizers: Patricia Hartge, Robert Hoover, Julie Palmer, James Cerhan, Anne Zeleniuch-Jacquotte, Michael Thun, Deborah Winn, Chinonye Harvey, and Geoffrey Tobias. *(Photograph Credit: Keith Richardson)*

DCEG *Linkage*

DCEG Linkage **is a publication of the Division of Cancer Epidemiology and Genetics, National Cancer Institute. The newsletter is available online at *http://www.dceg.cancer.gov.***

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genetic effects, such as those found by studying single nucleotide polymorphisms in genome-wide association studies (GWAS). Moreover, many of the cohort studies possess prediagnostic epidemiologic and biochemical data, which provide the opportunity to determine whether exposures, such as dietary intake, occurred before the onset of the cancer. For less common cancers, the consortium fosters the extensive collaborations necessary to gather a sufficient number of cases and statistical power to answer etiologic questions.

Consortium projects are in various stages of development, with some reporting results, others conducting analyses, and others newly forming. Among the early teams was the Breast and Prostate Cancer Cohort Consortium (BPC3), which identified a prostate cancer risk locus at chromosome 8q24. The BPC3 team also recently published a new GWAS report demonstrating multiple novel loci associated with prostate cancer (*Nat Genet* 2008;40:310–315). Such observations provide critical new insights into the underlying determinants of cancer, which may lead to better risk prediction models, improved screening and detection tools, and new therapeutic directions.

PanScan, a project team composed of 12 prospective epidemiologic cohorts, is making strides in its search for pancreatic cancer susceptibility genes. In 2008, the PanScan study team completed a whole-genome scan of 2,000 pancreatic cancer cases, which is currently being analyzed.

Also under way is the Vitamin D Pooling Project (VDPP). Epidemiologic evidence suggests that vitamin D deficiency is associated with increased risks of certain types of cancer, especially colorectal cancer. VDPP seeks to understand the relationship of vitamin D with the development of less common cancers, such as renal, gastric and esophageal, endometrial, ovarian, and pancreatic tumors as well as the lymphomas. Recently, assays measuring 25-hydroxyvitamin D [25(OH)D] on more than 11,000 samples from 10 participating cohorts were completed, and the findings will soon be published.

Although assembled with a focus on cancer, the consortium has the ability to study non-cancer outcomes as well. A project to take advantage of this data resource is the body mass index (BMI) pooling project. The BMI project contains data on several million Caucasian subjects from 26 cohorts; a parallel project will pool data on BMI and mortality in Asian cohorts. With large numbers of subjects, investigators hope to better clarify the relationship between being overweight and death rates for many conditions.

"The consortium meetings create the synergy and enthusiasm necessary to solve complex research questions," remarked Dr. Deborah Winn, Deputy Director of DCCPS. "The past, current, and future discoveries coming from the consortial projects will have major public health impacts."

A new project team focusing on breast cancer among African American women convened for the first time at the 2008 annual meeting. The investigators plan to conduct GWAS to clarify why African American women are more likely to be diagnosed with aggressive, high-grade, and estrogen- and progesterone-receptor–negative breast cancers.

The consortium is also supporting a newly formed brain cancer study group. The team will focus on glioma, an often-fatal cancer of unknown etiology,

although many studies suggest a familial component. Investigators hope that GWAS of this tumor using the 2,000 cases available within the consortium will yield important clues. The meeting also provided an opportunity for small group discussions focusing on several other cancers, including non-Hodgkin lymphoma and cancers of the upper gastrointestinal tract, liver, and endometrium.

Cross-cutting workshops are another key component of the annual consortium meetings. Dr. Julie Palmer from Boston University chaired a working group that discussed methodologic challenges, including a presentation by **Gabriella Andreotti, Ph.D.,** Occupational and Environmental Epidemiology Branch, on the collection of environmental samples. **Lindsay M. Morton, Ph.D.,** Radiation Epidemiology Branch, chaired a session on second cancers, while **Yikyung Park, Sc.D.,** Nutritional Epidemiology Branch, led a session on using cancer registries to ascertain cancer outcomes.

Strategic planning is vital as the consortium looks to the future. "One of the most exciting things about working with the consortium is to see the creativity and energy that the investigators are putting in to develop new directions and projects," observed **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program (EBP). "It is this momentum which continues to move the consortium forward." This year, 10 new project proposals were submitted for consideration to the consortium.

"One of the most satisfying parts of being involved with the creation and ongoing development of the consortium has been seeing investigators from all biomedical disciplines come together to work out these pressing research questions," noted **Robert N. Hoover, M.D., Sc.D.,** Director of EBP. As the consortium matures, investigators remain excited about the crucial and distinctive foundation it provides to foster studies that illuminate the causes of cancer using the power of collaboration, large sample sizes, and the unique properties of the cohort study design.

For more on the Cohort Consortium, visit http://epi.grants.cancer.gov/Consortia/cohort.html. ■

—Maria Sgambati, M.D.

NORMAN BOYD VISITS AS AN HREB DISTINGUISHED LECTURER

In November, the Hormonal and Reproductive Epidemiology Branch (HREB) hosted Dr. Norman F. Boyd, senior scientist at the Campbell Family Institute for Breast Cancer Research at the Ontario Cancer Institute and professor of medicine at the University of Toronto, as an HREB Distinguished Lecturer.

Gretchen Gierach, Louise Brinton, Norman Boyd, and Joseph Fraumeni.

Dr. Boyd's pioneering work in developing improved methods to identify components of breast tissue at increased risk of cancer, understanding the relationship between these components and other risk factors, and exploiting this information in the prevention of breast cancer has earned him international recognition.

During his visit, Dr. Boyd presented a seminar titled, "Breast tissue composition and susceptibility to breast cancer." He discussed potential mechanisms of breast cancer risk associated with mammographic density, a strong and independent risk factor for breast cancer. Dr. Boyd explained that mammographic density, which reflects variation in the tissue composition of the breast, is influenced by some hormones and growth factors as well as genetic factors. He proposed that cumulative "exposure" to mammographic density may be an important determinant of breast cancer incidence, such that differences in the rate of change in mammographic density earlier in life may be associated with subsequent breast cancer risk. To explore this hypothesis, Dr. Boyd is leading a study of women aged 15 to 30 in which hormone levels are related to a novel, quantitative measure of breast tissue composition by magnetic resonance imaging, which reflects the presence of fibroglandular and adipose tissue. Dr. Boyd concluded that there is a need for a better understanding of the potential biologic pathways and tissue components that contribute to mammographic density and its influence on breast cancer risk.

During the remainder of his visit, Dr. Boyd met with a number of NCI investigators in informal discussions. During a luncheon meeting, Dr. Boyd led a discussion with DCEG and Cancer Prevention Fellows on various issues related to career development. He also participated in a series of roundtable discussions. One session, led by HREB fellow **Gretchen L. Gierach, Ph.D., M.P.H.,** focused on evolving technologies to measure mammographic density, and another, led by **Mark H. Greene, M.D.,** Chief of the Clinical Genetics Branch, dealt with the genetic regulation of mammographic density.

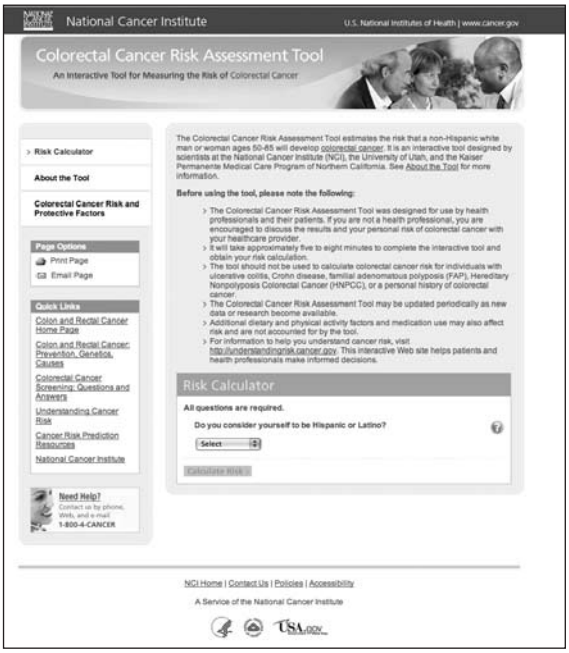
—Gretchen L. Gierach, Ph.D., M.P.H.

NEW TOOL PREDICTS COLORECTAL CANCER RISK

In 2008, nearly 149,000 Americans were diagnosed with colorectal cancer and almost 50,000 died from the disease, making it the third most commonly diagnosed cancer and the third leading cause of cancer mortality. Continuing the DCEG tradition of developing cancer risk prediction models, such as the "Gail model" for breast cancer, NCI staff has played a major role in developing the first tool that provides an absolute estimate of colorectal cancer risk in the U.S. population. The details of the statistical model appeared online in the *Journal of Clinical Oncology* in December. Using a respondent's answers to a few simple questions, this Web-based interactive tool estimates an individual's 5-year, 10-year, and lifetime risk of developing colorectal cancer.

Ruth M. Pfeiffer, Ph.D., a senior investigator in the Biostatistics Branch and senior author on the model's development and validation studies, explained that such a tool offers a variety of applications. "The model might be used by researchers to determine sample sizes and eligibility criteria for screening and prevention trials. The tool can also assist physicians in counseling their patients. Anybody can go to the Web site and plug in their individual data, but interpreting the results is best done in consultation with a health care professional."

Estimates of relative risks for the model were obtained using data from two large population-based case-control studies. "Because colorectal cancer occurs at three sites—the proximal colon, distal colon, and rectum—each with a different incidence rate, we assumed that some risk factors are probably different," explained Dr. Andrew Freedman, an epidemiologist in the NCI Division of Cancer Control and Population Sciences and lead author on the model's development.



The home page for the Colorectal Cancer Risk Assessment Tool, at http://wwwqa.cancer.gov/colorectalcancerrisk

"We created three different models for each sex, one for each site, and then combined them," he said. "We looked at all the known risk factors and picked out those that were most predictive." Age-specific baseline cancer hazard rates were estimated using NCI's Surveillance Epidemiology and End Results Program incident rates from 1992 to 2002, so the model is broadly applicable to the U.S. population.

The final step was to develop and refine a short, self-administered risk-assessment questionnaire that captures the information used in the models.

For men, the most pertinent factors affecting risk were a cancer-negative colonoscopy in the previous 10 years, history of colorectal cancer in first-degree relatives, a history of colon polyps, regular use of aspirin or other nonsteroidal anti-inflammatory drugs, cigarette smoking, body mass index, vigorous leisure-time activity, and vegetable consumption. Similar risk factors were seen in women, with the addition of hormone replacement therapy. After a user provides information about each of these factors, "the tool uses an algorithm to calculate the absolute risk, based on age and sex of the individual," Dr. Freedman explained.

Use of the model is currently limited to non-Hispanic white men and women aged 50 and older. "We had no data on individuals younger than 50 years, so the model starts at age 50, and we also had no data on minorities to provide reliable estimates of risks in these populations," Dr. Pfeiffer noted. "But efforts are ongoing to expand the model to include African Americans and other racial and ethnic groups."

The next step was to validate the model using an independent population. **Yikyung Park, Sc.D.,** a staff scientist in the Nutritional Epidemiology Branch and lead author on the validation study, expressed her excitement about using the prospective NIH-AARP Diet and Health Study cohort for this purpose. "This was an excellent use of this cohort, which has so many possible uses." She explained, "We validated the model in two ways. First, we used it to predict how many cases we would expect to find in the study population and compared that number to the actual number of cases observed in the

cohort. We found the fit to be very good. Second, we estimated the model's ability to predict risk on an individual level and found it to be modest, but similar to that of other absolute risk prediction cancer models."

Continuing the DCEG tradition of developing cancer risk prediction models, NCI staff has played a major role in developing the first tool that provides an absolute estimate of colorectal cancer risk in the U.S. population.

Dr. Pfeiffer explained, "It can predict the correct number of events overall but it cannot predict well which specific individuals will get cancer." She further noted that this is not a screening tool. "It can help a physician decide whether to screen or not, but it cannot replace a colonoscopy."

Dr. Freedman said that creating the tool was "a tremendous amount of work, but we were lucky to have an interdisciplinary collaborative team that worked very hard on this project. We all realized the importance this new tool will have for public health."

The Web-based tool can be found at http://wwwqa.cancer.gov/colorectal-cancerrisk. Similar tools developed by NCI investigators can be found for melanoma (www.cancer.gov/melanomarisktool), I-131 exposure (http://ntsi131.nci.nih.gov), and breast cancer (www.cancer.gov/bcrisktool). ■

—Terry Taylor, M.A.

NCI DIRECTOR'S INNOVATION AWARDS

In January, NCI Director John E. Niederhuber, M.D., presented the 2009 NCI Director's Intramural Innovation Awards at the 13th Annual NCI Intramural Scientific Retreat in Bethesda.

Designed to support the development of highly innovative approaches and technologies aimed at significant cancer-related problems, the awards offer one-time research funding at two levels: Principal Investigator (PI) Awards for tenure-track investigators or those tenured within the past five years and Career Development Awards for postdoctoral fellows, staff scientists, staff clinicians, or senior scientists. Funds are to be used during the current fiscal year.

Four DCEG investigators received PI Awards: **Christian C. Abnet, Ph.D., M.P.H.,** Nutritional Epidemiology Branch, for his proposal, "Search for a virus in esophageal squamous cell carcinoma from high-risk geographic regions"; **Ludmila Prokunina-Olsson, Ph.D.,** Laboratory of Translational Genomics (LTG), for "Detection of allele-specific physical interactions for cancer-associated genetic variants identified by genome-wide association studies"; **Sharon A. Savage, M.D.,** Clinical Genetics Branch, for "Evaluation of sub-telomeric methylation in the pathogenesis of dyskeratosis congenita, a cancer predisposition syndrome"; and **Rose Yang, Ph.D., M.P.H.,** Genetic Epidemiology Branch, for her proposal on "Genomic alterations in radiation-related breast cancer using array-CGH."

Two DCEG fellows received Career Development Awards: **Hye Kyung Kim, M.D.** (LTG), for her proposal on "MicroRNA single nucleotide polymorphisms in cancer susceptibility loci 8q24, 11q13, and 5p12," and **Jill Koshiol, Ph.D.,** Infections and Immunoepidemiology Branch, for "Chronic immune stimulation and lymphomagenesis."

Hye Kyung Kim, Ludmila Prokunina-Olsson, Sharon Savage, and Rose Yang are each shown receiving their awards from John Niederhuber.

DCEG WELCOMES VISITING SCHOLAR NORMAN BRESLOW

In October, DCEG welcomed Dr. Norman Breslow, professor and former chair of the Department of Biostatistics at the University of Washington School of Public Health and Community Medicine, as the third Visiting Scholar of 2008 in recognition of his leadership in biostatistics and cancer epidemiology. **Nilanjan Chatterjee, Ph.D.,** Chief of the Biostatistics Branch (BB), who was mentored by Dr. Breslow, hosted the visit along with the DCEG Office of Education.

Dr. Breslow is best known for his pioneering contributions to statistical methods in cancer epidemiology, particularly in survival analysis, case-control studies, overdispersed Poisson data, generalized linear mixed models, and two-phase designs. Among his many influential publications is the two-volume *Statistical Methods in Cancer Research,* through which Dr. Breslow and his coauthor, Dr. Nicholas Day, helped develop and popularize the use of statistical modeling in the analysis of case-control and cohort data. Dr. Breslow's honors include election into the Institute of Medicine of the National Academies, Honorary Fellowship in the Royal Statistical Society, Honorary Life Membership in the International Biometric Society, and, most recently, a historic interuniversity honorary doctorate issued by Hasselt University and the Catholic University of Leuven in Belgium.

After earning his doctoral degree in statistics from Stanford University in 1967, Dr. Breslow joined the Department of Biostatistics at the University of Washington, where in 1969, he joined the National Wilms Tumor Study (NWTS) Committee as a founding member. In this role, he established the NWTS Data and Statistical Center, which is now housed at the Fred Hutchinson Cancer Research Center and holds the largest collection of clinical data on Wilms tumor in the world.

Dr. Breslow is best known for his pioneering contributions to statistical methods in cancer epidemiology, particularly in survival analysis, case-control studies, overdispersed Poisson data, generalized linear mixed models, and two-phase designs.

In his Visiting Scholar seminar, Dr. Breslow described the history of the NWTS and provided a comprehensive overview of findings across the study's 40 years of follow-up. One of the first multidisciplinary collaborations in clinical oncology, the NWTS has enrolled more than 10,000 participants since 1985, representing about 70 percent of all Wilms tumor patients in North America. A particular focus of the study has been to identify low- and high-risk groups based on histology and stage of disease at diagnosis. Doing so has made it possible to reserve more aggressive treatments, associated with greater likelihood of secondary complications, for patients at greatest risk of relapse.

Dr. Breslow's presentation highlighted a number of analyses from the Late Effects Study related to mortality among Wilms tumor survivors as compared with national population rates, as well as the risks of serious medical conditions and adverse reproductive outcomes that are likely due either to treatment or to biological factors that contributed to the development of Wilms tumor. He also discussed analyses related to genetic heterogeneity and heritability and described recent efforts to incorporate biomarkers in epidemiologic data with laboratory findings.

Norman Breslow

Later that afternoon, Dr. Breslow met with DCEG investigators for a group discussion on childhood tumors and second cancers. Participants in the meeting included **Sharon A. Savage, M.D.,** and **Blanche P. Alter, M.D., M.P.H.,** both of the Clinical Genetics Branch, and **Preetha Rajaraman, Ph.D., Rochelle E. Curtis, M.A., Ruth A. Kleinerman, M.P.H.,** and **Lindsay M. Morton, Ph.D.,** of the Radiation Epidemiology Branch. Each investigator presented findings from an ongoing investigation, and Dr. Breslow offered insight into statistical methods, matching criteria, and exposure characterization.

The next day, Dr. Breslow led a seminar on efficient design and analysis for cohort and case-control studies. He expounded upon the analytic methods used in the NWTS and delved deeper into important methodological issues. He described two valuable new software applications that compute relative risks from two-phase designs: 1) the R package Survey created by Dr. Thomas Lumley of the University of Washington and 2) the R package NestedCohort (http://dceg.cancer.gov/tools/analysis/nested-cohort) developed by **Hormuzd A. Katki, Ph.D.** (BB), and Dr. Steven Mark, formerly of DCEG. Dr. Breslow emphasized the potential for estimating absolute and attributable risks as a major advantage of two-phase designs. These two measures of risk, which may be computed using the NestedCohort software, help assess the clinical and public health utility of epidemiologic findings.

Other statistical issues, including how to handle temporal variables, pooling of data from case-control and cohort studies, and the obstacles to broader use of multistage designs, were discussed in an afternoon meeting led by **Sholom Wacholder, Ph.D.** (BB), and Dr. Katki. Throughout Dr. Breslow's visit, he stressed that it is only after thorough consideration of the research question that one can begin to think about methodology.

The DCEG Office of Education hosted an informal lunch for Dr. Breslow and fellows in the Biostatistics Branch during which he answered questions about developing new methods, becoming an effective mentor and teacher, and finding balance between building strong scientific collaborations and conducting one's own research. In response to this last question, Dr. Breslow expressed appreciation for the NCI commitment to provide funding for statistical methods research. Dr. Breslow closed the session by emphasizing the integral role a postdoctoral fellowship can play in laying the foundation for an entire research career. During his visit, he remarked, "it is a pleasure to be here at DCEG where so many of our students have moved forward."

Dr. Wacholder, a graduate of the University of Washington biostatistics program, described Dr. Breslow as a "rigorous thinker, teacher, and writer," possessing the "kinds of qualities that make a true scholar." ■

—Lisa Prokop

CHANGING GUARD AT THE INSTITUTIONAL REVIEW BOARD

In January, **Maureen C. Hatch, Ph.D.,** Head of the Chornobyl Research Unit in the Radiation Epidemiology Branch, finished a two-year term as chair of the NCI Special Studies Institutional Review Board (SSIRB) and was succeeded by Dr. Nancy Potischman, a nutritional epidemiologist in the Applied Research Program of the Division of Cancer Control and Population Sciences. Dr. Hatch remains on the board as vice chair.

Maureen Hatch and Nancy Potischman

During Dr. Hatch's tenure—particularly the last 12 months—the board faced serious new challenges in weighing the risks and benefits to human subjects from the rapidly growing field of genetics. In this context, the NCI SSIRB addressed the ethical issues associated with genome-wide association studies (GWAS). For their work in this area, the SSIRB members received a 2008 NIH Director's Merit Award. In addition, Dr. Hatch; Lynn Sayers, the SSIRB Protocol Coordinator; **Susan Privot,** Office of the Director, the SSIRB Executive Secretary; and colleagues created an intranet Web site that provides investigators with descriptions, instructions, checklists, and links to other useful sites as an aid to navigating the process of submitting protocols for IRB review. Finally, Dr. Hatch initiated the practice of ending the board meetings with a general discussion of relevant journal articles in order to keep abreast of developments in human subjects protection.

Dr. Potischman will serve as chair of the SSIRB for the next three years. Her primary research efforts focus on the development of dietary assessment measurements, biomarkers of nutritional status, and hormonal factors related to cancer. Her work earned her an NIH Award of Merit in 2005 for promoting the science of energy balance and cancer and another in 2008 for advancing scientific rigor of dietary assessment in children and relating early-life exposures to cancer risk.

—Maureen C. Hatch, Ph.D.

NEW IMMUNITY AND INFLAMMATION PLANNING GROUP

At a recent DCEG Senior Advisory Group retreat, the group identified a number of broad areas of interest that are central in the Division's work to understand the etiology of cancer (see *Linkage,* November 2008). Toward this end, a series of planning groups was established to enable strategic planning in genome-wide association studies, environmental and dietary exposure assessment, development of mission-critical high-throughput laboratory services, biorepository enhancements, investigations into tumors that are highly lethal (e.g., liver cancer) or rising in incidence (e.g., thyroid cancer), and the role of inflammatory and immunological processes in carcinogenesis.

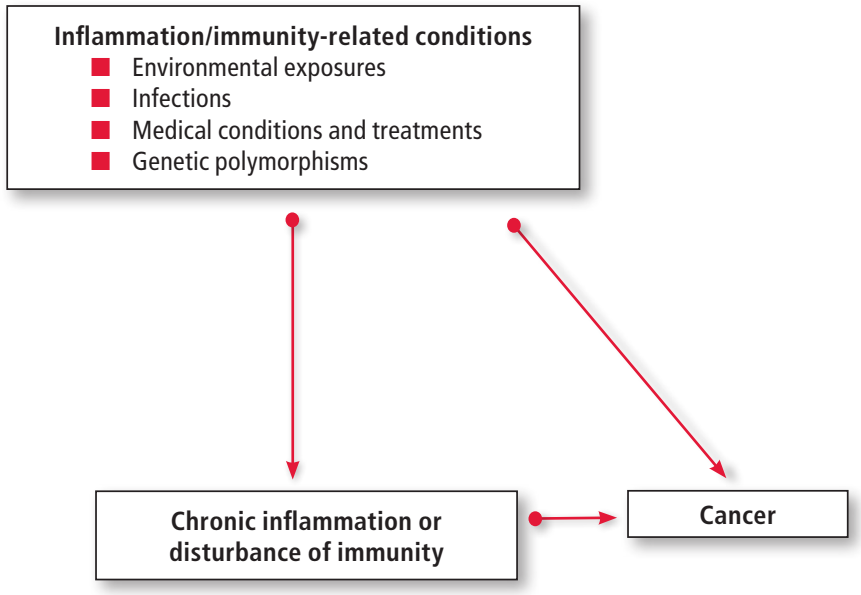


Figure 1. Proposed causal pathways of inflammation to cancer.

Altered immunity and chronic inflammation appear to play a key role in the etiology of several malignancies. A number of cancers are directly linked to oncogenic viruses and bacteria. Immunosuppression results in poor control of these infections, in some cases dramatically amplifying cancer risk (e.g., Epstein-Barr virus and certain lymphomas; human herpesvirus 8 and Kaposi sarcoma). In other cases, infection-associated inflammation is crucial to the development of cancer (e.g., hepatitis C virus and hepatocellular carcinoma; *Helicobacter pylori* and gastric cancer). Immune disturbances and chronic inflammation are also implicated in other malignancies not associated with infections. For example, chronic autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosis, and Sjögren's syndrome are associated with increased risk of non-Hodgkin lymphoma, likely due to chronic immune activation. Tuberculosis and pulmonary scarring have been linked to an increased risk of lung cancer, while use of non-steroidal anti-inflammatory drugs appears to reduce colon cancer risk. Polymorphisms in genes related to immunity and inflammation have been associated with altered susceptibility to several malignancies.

The committee has identified important gaps in knowledge, which may serve as opportunities for collaborative research involving epidemiologists and laboratory scientists.

DCEG is conducting a strategic planning process to coordinate the Division's molecular epidemiology research activities in this important area. The process is coordinated by the Inflammation, Immunity, and Cancer Steering Committee, cochaired by **Eric A. Engels, M.D., M.P.H.,** Infections and Immunoepidemiology Branch (IIB), and **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program. Other members include **James J. Goedert, M.D.** (IIB), **Allan Hildesheim, Ph.D.** (Chief of IIB), **Ann W. Hsing, Ph.D.,** Hormonal and Reproductive Epidemiology Branch (HREB), **Martha S. Linet, M.D., M.P.H.,** Chief of the Radiation Epidemiology Branch, **June A. Peters, M.D., C.G.C.,** Clinical Genetics Branch, **Ruth M. Pfeiffer, Ph.D.,** Biostatistics Branch, **Ligia A. Pinto, Ph.D.** (IIB), **Mark Purdue, Ph.D.,** Occupational and Environmental Epidemiology Branch, and **Sophia S. Wang, Ph.D.** (HREB).

The committee has identified important gaps in knowledge, which may

serve as opportunities for collaborative research involving epidemiologists and laboratory scientists. Measurement of tumor-related inflammatory processes is difficult due to the inaccessibility of these tissues for sampling. The precise inflammatory and immune pathways that connect predisposing disease states (e.g., infections and autoimmune diseases) to cancer remain to be elucidated (see figure 1). The biological effects of common genetic polymorphisms on the immunological and inflammatory response are unknown.

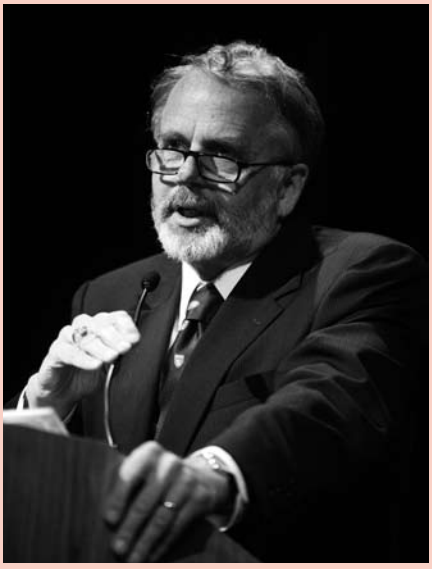
To address these questions and facilitate epidemiologic investigations, the steering committee established working groups in four specific areas. These groups have recruited investigators from across the Division and will continue to serve as a forum for communication, planning, and collaboration. One group is engaged in the development and validation of a panel of blood biomarkers of the immune/inflammatory response, suitable for large-scale multiplex assessment. A second group is coordinating efforts to optimize tissue markers that can be utilized in the molecular evaluation of tumors in epidemiologic studies. Another working group is summarizing DCEG's portfolio of linked registry resources that can be used for new studies of immune-related medical conditions in association with cancer risk. A fourth working group provides a forum for investigating the interface of environmental and biobehavioral risk factors with chronic inflammation, altered immunity, and cancer.

Finally, in developing a program of molecular epidemiology in this area, the planning group will coordinate efforts and seek out collaborations with immunologists in the Center for Cancer Research and the recently developed NIH Center for Human Immunology. The intramural clinics and laboratory sciences at NIH are rich in the field of immunology, and their contributions will be critical to the success of interdisciplinary population-based studies in this area. ■

—Eric A. Engels, M.D., M.P.H.

ROBERT HOOVER TESTIFIES ON CELL PHONE USE

In September, the Subcommittee on Domestic Policy of the U.S. House of Representatives' Committee on Oversight and Government Reform held a hearing titled "Cell phone use and tumors: What the science says." The hearing was called in response to concerns that exposure to cell phones might cause brain tumors. The subcommittee invited **Robert N. Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, to join a panel of witnesses that included Julius Knapp, Director of the Office of Engineering and Technology at the Federal Communications Commission, Dr. David O. Carpenter, Director of the Institute for Health and the Environment at the University at Albany, Dr. Ronald B. Herberman, Director of the University of Pittsburgh Cancer Institute, and Ellen Marks, an advocate from California.



Robert Hoover

The panel of witnesses discussed current research on cell phone use and tumor incidence. Most concern focused on the potential health effects of radiofrequency waves emitted by cell phones, especially for childhood exposures.

Dr. Hoover summarized findings from large-scale epidemiological investigations, indicating that so far, no conclusive evidence has linked cell phone use to the development of brain tumors. He further noted that there has been "no meaningful increase in the incidence of brain or other nervous system cancers from 1987 through 2005, a time period when cell phone use increased 10-fold."

Dr. Hoover also discussed limitations to current research and the need for future investigations to examine the effects of long-term use (more than 10 years), new cell phone technology, and exposure in children. His concluding statements underscored the importance of providing the public with information on what is and is not known in science. He stressed that individuals may make behavioral decisions based on their own personal views of when to involve a "cautionary principle." However, a higher standard is called for in official public health recommendations, which must be based on an objective assessment of the weight of the scientific evidence.

The testimony from the panel of witnesses will be used to help determine whether legislation is necessary.

—Cherie M. Vitartas, M.P.H.

STEPHEN RAPPAPORT VISITS DCEG AS DISTINGUISHED LECTURER

In December, the Occupational and Environmental Epidemiology Branch (OEEB) hosted Dr. Stephen M. Rappaport, professor of environmental health at the University of California, Berkeley, as an OEEB Distinguished Lecturer in Occupational and Environmental Cancer.

Mary Ward, Stephen Rappaport, and Debra Silverman.

Dr. Rappaport is internationally recognized for his pioneering work in developing and applying biomarkers of exposure to toxic chemicals, including benzene and polycyclic aromatic hydrocarbons. He uses environmental measurements and biomarkers to elucidate the metabolism of toxic chemicals and to quantify inter-individual variability in biomarker levels. He has published extensively in the assessment of long-term chemical exposures for purposes of investigating controlling workplace hazards and exposure-response relationships. He also co-authored the definitive textbook *Quantitative Exposure Assessment.* Currently, Dr. Rappaport is the principal investigator of the new NIH-funded Biological Response Indicators of Environmental Stress Center, a multidisciplinary program project that brings together researchers from public health, chemistry, and electrical engineering to develop the latest generation of biomarkers and biosensors.

During his seminar, titled "Using environmental measurements and biomarkers to investigate metabolism of benzene," Dr. Rappaport discussed his findings from studies of benzene-exposed workers conducted in China in collaboration with DCEG and other scientists. He presented analyses using biomarkers of exposure to determine the influence of external chemical exposure as well as the relationship with covariates such as gender; age; and genetic, physiological, and lifestyle factors. Such analyses provide valuable insights into the sources of inter-individual differences in important processes governing rates of uptake and metabolism. His presentation showed how such joint exposure/biomarker studies have advanced our understanding of the metabolism of benzene, a ubiquitous environmental chemical that damages bone marrow and causes leukemia, and how current benzene risk assessments may substantially underestimate leukemia risks among low-exposed and susceptible subjects.

Dr. Rappaport is internationally recognized for his pioneering work in developing and applying biomarkers of exposure to toxic chemicals, including benzene and polycyclic aromatic hydrocarbons.

Dr. Rappaport also presented a seminar titled "Protein adducts as biomarkers of exposure: Possibilities for the future" to OEEB staff and met with a number of DCEG investigators for informal discussions. He discussed his ongoing collaborations with **Qing Lan, M.D., Ph.D., M.P.H.,** and **Nathaniel Rothman, M.D., M.P.H., M.H.S.,** on biomarker studies in China and with **Joanne S. Colt, M.P.H., M.S., Jay Nuckols, Ph.D.,** and **Mary H. Ward, Ph.D.,** on the Northern California Childhood Leukemia Study and Fresno Exposure Study. He also met with investigators from the Agricultural Health Study, **Michael C.R. Alavanja, Dr.P.H., Aaron E. Blair, Ph.D., M.P.H., Laura Beane-Freeman, Ph.D.,** and **Joseph B. Coble, Sc.D.,** to discuss using biomarkers for pesticide exposure assessment in future studies. In addition, Dr. Rappaport held a luncheon discussion with pre- and postdoctoral fellows during which he advised on research strategies and early career development. ■

—Mary H. Ward, Ph.D.

NIH RESEARCH FESTIVAL

The 21st annual NIH Research Festival was held in October. This intramural event provides a venue for NIH and NCI investigators to showcase their achievements and to explore the innovative research being conducted throughout the NIH Intramural Research Program. DCEG had a substantial presence at this year's event, with many investigators chairing sessions or presenting posters.

Sharon A. Savage, M.D., Clinical Genetics Branch (CGB), organized and chaired the symposium "Telomeres: The transition from basic science to clinical medicine." The session highlighted new findings in telomeric repair, telomeres in T cells, and mutations in telomere genes and human disease, as well as the application of telomere length in clinical and epidemiology studies. During the session, Dr. Savage spoke on "Genetic epidemiology of telomeres," and **Blanche P. Alter, M.D., M.P.H.** (CGB), presented "Using telomere length to diagnose dyskeratosis congenita."

Ola Landgren, M.D., Ph.D., an investigator in the Genetic Epidemiology Branch (GEB), and Dr. Charles Rotimi of the National Human Genome Research Institute cochaired the symposium "Racial disparities in chronic disease: Clues to pathogenesis." The session discussed opportunities to study variable drug response and pathogenesis based on differential distribution of diseases by ethnicity and ancestry. During the session, Dr. Landgren presented "Racial disparity patterns for multiple myeloma and its precursor, monoclonal gammopathy of undetermined significance, provide novel clues to pathogenesis."

The following DCEG investigators presented posters: **Porcia Bradford, M.D.** (GEB), on "Cutaneous lymphoma incidence patterns in the United States: A population-based study of 4,064 cases"; **Linda Dong, Ph.D.,** Occupational and Environmental Epidemiology Branch (OEEB), on "Comprehensive analysis of candidate growth, differentiation and apoptosis genes with risk of renal cancer in the Central and Eastern European Renal Cancer Study"; **Vladimir Drozdovitch, Ph.D.,** Radiation Epidemiology Branch (REB), on "Collection and use of individual behavioral and consumption rate data to improve reconstruction of thyroid doses from nuclear weapons tests in Kazakhstan"; **Neal D. Freedman, Ph.D., M.P.H.,** Nutritional Epidemiology Branch, on "Cigarette smoking and subsequent risk of lung carcinoma in men and women"; **H. Dean Hosgood, III, Ph.D.** (OEEB), on "Portable stove intervention reduces lung cancer mortality risk in lifetime smoky coal users"; **Sara Karami, M.P.H.** (OEEB), on "Genetic variation within the vitamin D pathway modifies renal cell carcinoma risk"; **Jill Koshiol, Ph.D.** (GEB), on "Human papillomavirus is absent from esophageal cancer in China"; **Kyoung-Mu Lee, Ph.D.** (OEEB), on "Differential effects of smoking on lung cancer mortality before and after household stove improvement in Xuanwei, China"; **Qizhai Li, Ph.D.,** Biostatistics Branch, on "Robust genome-wide association studies"; **Xueying Liang, Ph.D.** (GEB), on "Common genetic variants in candidate genes and risk of familial lymphoma"; **Gwen Murphy, Ph.D., M.P.H.,** Infections and Immunoepidemiology Branch, on "Epstein-Barr virus and gastric adenocarcinoma: A meta-analysis"; **Ludmila Prokunina-Olsson, Ph.D.,** Laboratory of Translational Genomics, on "From genome-wide association studies to molecular phenotypes: A novel SNP within the *IGF2BP2* gene is associated with type 2 diabetes and expression of a functional splice form"; and **Chu-Ling Yu, Sc.D.** (REB), on "Assessment of lifetime cumulative sun exposure using self-administered questionnaire: Reproducibility of two approaches." ■

—Cherie M. Vitartas, M.P.H.

NEIL CAPORASO HONORED FOR COLLABORATION

In October, **Neil E. Caporaso, M.D.,** Genetic Epidemiology Branch, gave a talk on "Genetic aspects of chronic lymphocytic leukemia (CLL) and the precursor condition, monoclonal B-cell lymphocytosis" at the International CLL Workshop held at the Mansoura Oncology Centre in Egypt. At the meeting, he was given an award by the President of Mansoura University, Dr. Ahmed B. Shehab El-Din, in appreciation of his collaboration with the International CLL group.

Neil Caporaso receives award from Ahmed Shehab El-Din, Hasan Abdel (Director of Mansoura Oncology Centre), and Ashraf Abdel Bacet (Vice Dean for Education and Student Affairs).

FRONTIERS IN CANCER PREVENTION MEETING

DCEG researchers were well represented during the Seventh Annual AACR International Conference on Frontiers in Cancer Prevention in Washington, DC, in November. This year's program highlighted the role of tissue injury, stem cells, infection, novel chemopreventive agents, molecular targeting, clinical trials, obesity, and behavioral research in cancer prevention. The plenary sessions focused on molecular targets in cancer prevention, international cancer prevention, tumor microenvironment and inflammation, communications, and integrative prevention.

DCEG researchers were featured in several key sessions. **Mitchell H. Gail, M.D., Ph.D.,** a senior investigator in the Biostatistics Branch, compared the discriminatory accuracy of the Breast Cancer Risk Assessment Tool (BCRAT) to a model including risks reported from seven single nucleotide polymorphisms (SNPs) associated with breast cancer. He found little improvement in discriminatory accuracy from adding the seven SNPs to BCRAT. **Sara Karami, M.P.H.,** a doctoral student in the Occupational and Environmental Epidemiology Branch (OEEB), evaluated the relation of genetic variation in the intracellular vitamin D receptor and other pathway genes to renal cell carcinoma etiology. During a press conference on renal cell carcinoma, **Lee E. Moore, Ph.D.,** a tenure-track investigator in OEEB, fielded questions on her finding that lipid metabolism-peroxidation genes modify susceptibility to sporadic kidney cancer, particularly cases that are not explained by known risk factors such as obesity, hypertension, and smoking.

Stephen J. Chanock, M.D., Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, spoke on the promise of genome-wide association studies in discovering new regions on the genome that are associated with specific diseases and traits, exploring new candidate genes and pathways in disease etiology, and making individual and public health decisions utilizing genetic markers for prediction of disease risk.

Challenging recent conventional thinking, **Eric A. Engels, M.D., M.P.H.,** a senior investigator in the Infections and Immunoepidemiology Branch, gave several reasons why using sensitive molecular techniques, such as polymerase chain reaction, may not suffice in proving causal relationships between viruses and cancer. He emphasized the importance of traditional epidemiologic studies in complementing laboratory investigations.

Jackie A. Lavigne, Ph.D., M.P.H., Chief, Office of Education (OE), presented training opportunities in the Division as part of a special session on NCI Opportunities for Junior Investigators. Dr. Jonathan S. Wiest, Director of the new NCI Center for Cancer Training, led the panel discussion with assistance from Dr. Jessica M. Faupel-Badger, Assistant Director for the NCI Cancer Prevention Fellowship Program. To complement this session, **Kristin Kiser, M.H.A.,** Fellowship Coordinator for OE, staffed the DCEG exhibit and spoke to graduate students about fellowships in DCEG.

In addition to speakers, DCEG staff were well represented in the poster sessions. Among the 26 poster presenters, some had been invited, including Scholar-in-Training Award recipient **Neal D. Freedman, Ph.D., M.P.H.,** a postdoctoral fellow in the Nutritional Epidemiology Branch. His poster was titled "Association of menstrual and reproductive factors with the risk of upper gastrointestinal tract cancers in the NIH-AARP cohort." ■

—Kristin Kiser, M.H.A.

DCEG Presenters: Eric Engels, Sara Karami, Jackie Lavigne, and Lee Moore. *(Photograph Credit: ©2008 AACR/Todd Buchanan)*

THE ALL-IRELAND CANCER CONFERENCE

In December, DCEG scientists joined cancer researchers from Ireland and the United Kingdom for the fourth All-Ireland Cancer Conference, held by the Ireland-Northern Ireland-NCI Cancer Consortium. The consortium, established in 1999, aims to reduce the burden of cancer in Ireland through scientific collaborations with NCI. This year's conference, held in Dublin, covered a range of topics from patient care to genome-wide association studies (GWAS).

Robert Hoover, Richard Hayes, and Stephen Chanock defend the epidemiologic and genetic ramparts at the All-Ireland Cancer Conference.

Stephen J. Chanock, M.D., Director of the Core Genotyping Facility and Chief of the Laboratory of Translational Genomics, **Robert N. Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program, and **Richard B. Hayes, D.D.S., Ph.D.,** senior investigator in the Occupational and Environmental Epidemiology Branch, presented a session on "State of the science: Cancer genomics and genome-wide association studies." Dr. Chanock, who chaired the session, provided an overview of GWAS in which he described recent discoveries by the NCI Cancer Genetic Markers of Susceptibility project, the challenges encountered in genetic mapping of cancer susceptibility, and the future promise afforded by studies of germline genetic variation in disease risk. Dr. Hoover followed with a discussion on genetic and non-genetic risk factors associated with breast cancer, including the role of hormones in breast cancer risk as well as findings from GWAS on gene regions associated with breast cancer. Dr. Hayes concluded by presenting advances in genetics research on colon and rectal cancer risk, such as the discovery of 8q24 and other colorectal cancer–associated gene regions.

Dr. Chanock provided an overview of genome-wide association studies in which he described recent discoveries by the NCI Cancer Genetic Markers of Susceptibility project, the challenges encountered in genetic mapping of cancer susceptibility, and the future promise afforded by studies of germline genetic variation in disease risk.

Later in the week, Drs. Chanock and Hoover taught a Cancer Genomics Master Class at the Institute of Molecular Medicine, St. James's Hospital and Trinity College Dublin. Dr. Chanock presented "The devil is in the DNA: The power of cancer genomics," and Dr. Hoover spoke on "The evolution of epidemiological research, from cottage industry to 'big science.'"

Dr. Hoover stated that his personal highlight from the conference was the presentations made by the young scientists from Ireland and NCI. He was very encouraged by their enthusiasm and the collaboration of individuals from Northern Ireland and the Republic of Ireland toward a unified goal of improving cancer outcomes. Many NCI postdoctoral fellows attended the conference, including **Gwen Murphy, Ph.D., M.P.H.,** a native of Ireland and a visiting fellow in the Infections and Immunoepidemiology Branch (IIB), and Dr. Lesley Anderson, a former IIB cancer prevention fellow, both of whom presented work from their fellowship experience at NCI. ■

—Cherie M. Vitartas, M.P.H.

DCEG FELLOWS AWARD FOR RESEARCH EXCELLENCE

The DCEG Fellows Award for Research Excellence (D-FARE) is a travel award offered for the professional development of young scientists in the Division.

The award, initiated by the DCEG Office of Education Advisory Group, recognizes fellows who have made exceptional contributions to scientific research projects. The contributions can include formulating the idea, study design, fieldwork, analysis, or interpretation of results, and the fellow must have had a major role in drafting a manuscript. Special consideration is given to projects in which fellows demonstrate growth beyond the discipline of their previous training. This year, four D-FARE winners will receive $1,500 each for travel to present their research at a scientific meeting.

D-FARE Winners: Huilin Li, Jill Koshiol, Idan Menashe, and Dean Hosgood.

Attendance at scientific meetings is critical to the fellowship experience, and the competition allows a greater number of fellows to participate in meetings, exposing them to important new scientific developments and permitting them to make vital connections with other scientists.

A group of senior DCEG scientists judged the submissions and made recommendations to the DCEG Director, who decided on the winners. Awards were announced in October, and funds must be used by the end of the fiscal year.

The winners are as follows:

- **H. Dean Hosgood, III, Ph.D.,** Occupational and Environmental Epidemiology Branch: *Association between genetic variants in VEGF, ERCC3, and occupational benzene hematotoxicity.*
- **Jill Koshiol, Ph.D.,** Infections and Immunoepidemiology Branch: *Evaluation of the presence and functionality of human papillomavirus in esophageal squamous cell carcinoma in Linxian, China.*
- **Huilin Li, Ph.D.,** Biostatistics Branch (BB): *Covariate adjustment and ranking methods to identify regions with high and low mortality rates.*
- **Idan Menashe, Ph.D.** (BB): *Do disparate outcomes after diagnosis explain Black-White racial disparity in breast cancer mortality?* ■

NEW SENIOR INVESTIGATORS

NIH recently awarded scientific tenure to **Qing Lan, M.D., Ph.D., M.P.H.,** of the Occupational and Environmental Epidemiology Branch, and **Katherine A. McGlynn, Ph.D., M.P.H.,** of the Hormonal and Reproductive Epidemiology Branch.

Katherine McGlynn and Qing Lan

Dr. Lan's research focuses on molecular epidemiologic studies of populations with occupational and environmental exposure to chemicals that are known or suspected carcinogens. She has carried out extensive studies of indoor air pollution, genetic susceptibility, and lung cancer among women in Asia, with a particular emphasis on exposure to polycyclic aromatic hydrocarbons. She has also studied genetic susceptibility and intermediate endpoints for non-Hodgkin lymphoma and leukemia, as well as the hematologic, immunologic, and genotoxic effects of workplace exposure to benzene, formaldehyde, and trichloroethylene. She received her doctoral degree in molecular epidemiology at the Chinese Academy of Preventive Medicine in Beijing as part of a joint training program with the U.S. Environmental Protection Agency and the University of North Carolina at Chapel Hill and her master's degree from the Johns Hopkins Bloomberg School of Public Health.

Dr. McGlynn's main research interests are the epidemiology of testicular cancer and related conditions as well as the epidemiology of liver cancer. To examine the etiology of testicular cancer, she conducted a large case-control study within the U.S. military population focused on early-life exposures and endocrine-disrupting chemicals. Her liver cancer research has examined co-factors for hepatocarcinogenesis among high-risk populations in China and factors related to the increasing incidence of liver cancer in the United States. Prior to joining DCEG, she received her doctoral degree in epidemiology from the University of Pennsylvania and her master's degree from Tulane University.

DYSKERATOSIS CONGENITA: FIRST NIH CLINICAL RESEARCH WORKSHOP

In September, the first NIH Clinical Research Workshop on Dyskeratosis Congenita (DC) was held. Organized by **Sharon A. Savage, M.D.,** of the Clinical Genetics Branch (CGB), and cosponsored by the NIH Office of Rare Diseases, the meeting focused on bringing clinicians and scientists studying DC together with affected patients and families in order to share recent findings, explore opportunities for future research, and empower patients with DC and their families to organize a support group.

DC is an inherited bone marrow failure and cancer predisposition syndrome characterized by exceedingly short germline telomeres. About half the patients with this multisystem disorder have mutations in telomere biology genes (see figure 1). Patients with DC are being studied in NCI's Inherited Bone Marrow Failure Syndromes study (http://marrowfailure.cancer.gov). Recent advances in understanding the molecular pathogenesis of DC include the discovery of new causative genes and the development of a diagnostic test. These developments, coupled with the need for a DC-specific family support group expressed by families participating in the NCI study, prompted this workshop.

Mark H. Greene, M.D., Chief of CGB, welcomed 80 participants, including clinicians, scientists, and 42 family members representing 17 families. Presentations by **Blanche P. Alter, M.D., M.P.H., Neelam Giri, M.D.** (both of CGB), Dr. Savage, and other investigators from the United States and Europe covered clinical findings, diagnosis, management, and genetic characterization of DC. Patients and families met with representatives from several other family support and advocacy groups and created a mission statement, action plan, and board of directors. Additional information about the DC family support group can be found at www.dcoutreach.com.

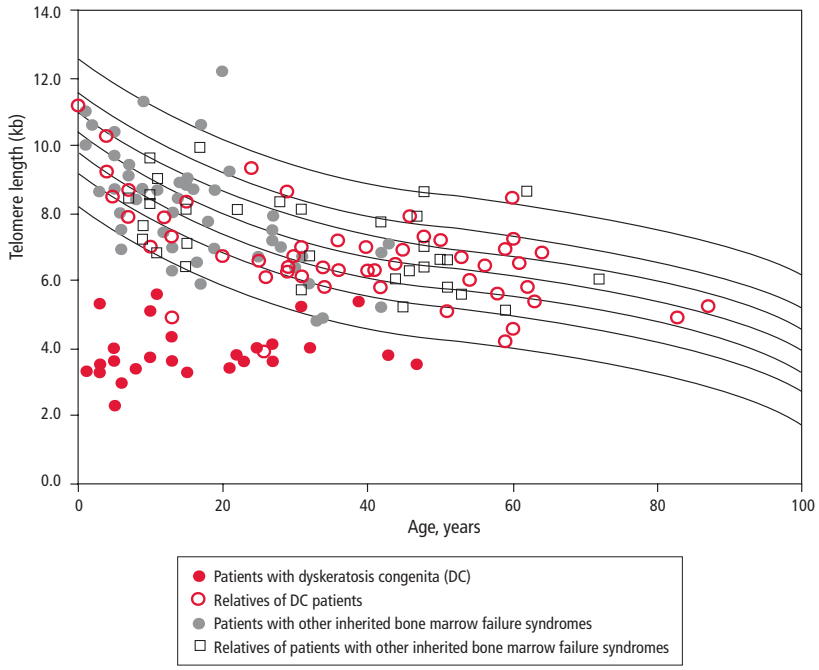


Figure 1. Telomere length measurement by flow-FISH (flow cytometry with multicolor fluorescence *in situ* hybridization) of leukocyte subsets is sensitive and specific for dyskeratosis congenita (DC). The 1st percentile (bottom line) and the 99th percentile (top line) were derived from 400 controls.

The workshop resulted in the formation of collaborative studies involving the clinical, scientific, and patient communities. The research strategies will be key in advancing scientific understanding of the molecular pathogenesis of DC and telomere biology, as well as improving therapeutic options for patients with DC. A future meeting will focus on developing consensus treatment guidelines. ■

—June A. Peters, M.S., C.G.C.

Larry Chloupek, deputy manager for the DCEG Administrative Resource Center (ARC), has left to take a position as the administrative liaison for the NIH Office of Intramural Research. He has worked at NCI for the last 17 years in various facets of administration. While in DCEG from 2001 through 2008, he specialized in human resources planning and coordinating space for the ARC and the Division. As a former personnel management specialist, he brought a wealth of expertise and knowledge to this role. Additionally, he guided the Division through many complicated moves, including an expansion at Executive Plaza South. "We wish him well in his new position," said Donna Siegle, Director, Office of Administrative Services.

Larry Chloupek competing in the 2008 NIH Relay

SCIENTIFIC HIGHLIGHTS

BREAST CANCER

Age-related Incidence Rate Crossover

Although breast cancer incidence is higher among black than white women under age 40, the reverse is true among older women. To quantify this crossover, data for 440,653 women diagnosed with invasive breast cancer from NCI's Surveillance, Epidemiology, and End Results (SEER) database from 1975 through 2004 were examined (see figure 1). Age-specific incidence rates overall (expressed as number of breast cancers per 100,000 woman-years) were higher among black (15.5) than white (13.1) women younger than 40 years and higher among white (281.3) than black (239.5) women aged 40 years or older. The black-to-white incidence rate crossover was observed more so for those with low-risk disease than for those with high-risk disease. In addition, the crossover occurred at earlier ages of diagnosis for low-risk than for high-risk tumor characteristics. **(Anderson WF, Rosenberg PS, Menashe I, Mitani A, Pfeiffer RM. Age-related crossover in breast cancer incidence rates between black and white ethnic groups. *J Natl Cancer Inst* 2008;100:1804–1814)**

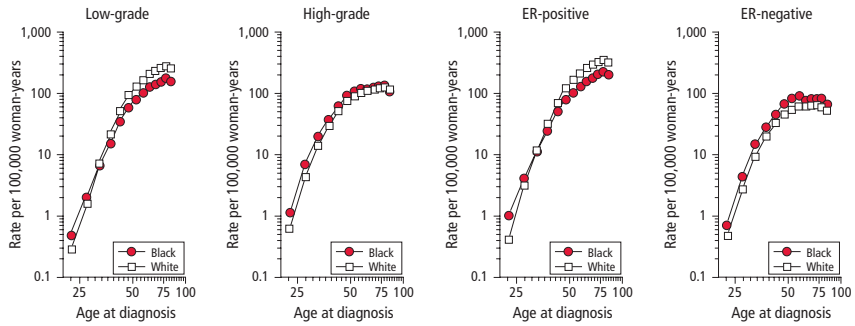


Figure 1. Incidence rate crossover between black and white women stratified by tumor characteristics (tumor grade and ER status) in NCI's Surveillance, Epidemiology, and End Results 9 Registries database from 1975 through 2004. The crossover was observed more so for those with low-risk disease (low-grade tumor or ER-positive status) than for those with high-risk disease (high-grade tumor or ER-negative status). (ER = estrogen receptor) (Anderson WF, et al. 2008)

Risk Factors for Male Breast Cancer

In the prospective NIH-AARP Diet and Health Study, breast cancer developed in 121 of 324,920 men studied. Men who reported a first-degree relative with breast cancer had an increased risk of breast cancer (relative risk [RR] = 1.92). Increased risk was also associated with a history of a bone fracture (RR = 2.20), obesity (RR = 1.79 for body mass indices of 30 vs. < 25 kg/m^2), and low physical activity, even after adjustment for body mass index. Smokers were at somewhat elevated risk, although trends were inconsistent. Alcohol consumption was not related to risk. The identified risk factors show some commonalities with female breast cancer. Differences may reflect unique mechanisms associated with androgens and their ratio to bioavailable estrogens. **(Brinton LA, Richesson DA, Gierach GL, Lacey JV Jr, Park Y, Hollenbeck AR, Schatzkin A. Prospective evaluation of risk factors for male breast cancer. *J Natl Cancer Inst* 2008;100:1477–1481)**

CERVICAL CANCER

Immune and DNA Repair Genes

Host genetic factors possibly related to persistence of human papillomavirus (HPV) infection and progression to cervical intraepithelial neoplasia grade 3 (CIN3) and cancer were examined. The authors genotyped 92 single nucleotide polymorphisms (SNPs) from 49 candidate immune response and DNA repair genes obtained from 469 women with CIN3 or cancer, 390 women with persistent HPV infections (median duration = 25 months), and 452 random control subjects from the 10,049-woman Guanacaste Costa Rica Natural History Study. A SNP in the Fanconi anemia complementation group A gene *(FANCA)*, G501S, was associated with increased risk of CIN3 or cancer. The AG and GG genotypes had a 1.3-fold and 1.7-fold increased risk for CIN3 and cancer, respectively (p for trend = 0.008; referent, AA). The *FANCA* haplotype that included G501S also conferred increased risk of CIN3 or cancer, as did a different haplotype that included two other *FANCA* SNPs (G809A and T266A). A SNP in the innate immune gene *IRF3* (S427T) was associated with increased risk of HPV persistence. Results support the role of *FANCA* variants in cervical cancer susceptibility and *IRF3* in HPV persistence. **(Wang SS, Bratti MC, Rodríguez AC, Herrero R, Burk RD, Porras C, González P, Sherman ME, Wacholder S, Lan ZE, Schiffman M, Chanock SJ, Hildesheim A. Common variants in immune and DNA repair genes and risk for human papillomavirus persistence and progression to cervical cancer. *J Infect Dis* 2009;199:20–30)**

CHILDHOOD CANCER

Prenatal and Perinatal Risk Factors

Prenatal, perinatal, and neonatal risk factors for neuroblastoma were investigated by linking 245 pediatric cases diagnosed between 1973 and 2005 in the Swedish Cancer Register to five controls per case from the Swedish Medical Birth Register. Increased risks were associated with maternal anemia during pregnancy (odds ratio [OR] = 2.95), neonatal respiratory distress (OR = 3.61), and low one-minute Apgar score (OR = 2.23) among cases diagnosed before one year of age, but not among older cases. **(Bluhm E,**

McNeil DE, Cnattingius S, Gridley G, El Ghormli L, Fraumeni JF Jr. Prenatal and perinatal risk factors for neuroblastoma. *Int J Cancer* 2008;123:2885–2890)

HEMATOPOIETIC MALIGNANCIES

Risks with Viral and Alcoholic Hepatitis

The authors evaluated risks of hematopoietic malignancies by subtype with prevalent hepatitis C virus (HCV), hepatitis B virus (HBV), and alcoholic hepatitis among 61,464 cases (aged ≥ 67) with hematopoietic malignancies and 122,531 population-based controls, frequency matched by gender, age, and year (1993–2002), from the SEER-Medicare database. HCV, HBV, and alcoholic hepatitis were reported in 195 (0.3%), 111 (0.2%), and 404 (0.7%) cases and 264 (0.2%), 242 (0.2%), and 798 (0.7%) controls, respectively. HCV was associated with increased risk of diffuse large B-cell lymphoma (OR = 1.5), Burkitt lymphoma (OR = 5.2), follicular lymphoma (OR = 1.9), marginal zone lymphoma (OR = 2.2), and acute myeloid leukemia (OR = 1.5, CI = 1.0–2.4). In contrast, HBV was unrelated to any hematopoietic malignancies. Alcoholic hepatitis was associated with decreased risk of non-Hodgkin lymphoma (NHL) overall but increased risk of Burkitt lymphoma. HCV may induce lymphoproliferative malignancies through chronic immune stimulation. **(Anderson LA, Pfeiffer R, Warren JL, Landgren O, Gadalla S, Berndt SI, Ricker W, Parsons R, Wheeler W, Engels EA. Hematopoietic malignancies associated with viral and alcoholic hepatitis. *Cancer Epidemiol Biomarkers Prev* 2008;17:3069–3075)**

LUNG CANCER

Inhaled Arsenic among Copper Smelter Workers

In a study of the relationship between respiratory cancer mortality and cumulative inhaled arsenic exposure in a cohort of copper smelter workers, the association between respiratory cancer and cumulative arsenic exposure was consistent with linearity within categories of arsenic concentration. The slope of the linear relationship with cumulative exposure increased with increasing arsenic concentration category. Results suggest a direct concentration effect from inhaled inorganic arsenic, whereby the excess relative risk for a fixed cumulative exposure was greater when delivered at a higher concentration and shorter duration than when delivered at a lower concentration and longer duration. **(Lubin JH, Moore LE, Fraumeni JF Jr, Cantor KP. Respiratory cancer and inhaled inorganic arsenic in copper smelters workers: A linear relationship with cumulative exposure that increases with concentration. *Environ Health Perspect* 2008;116:1661–1665)**

Menstrual and Reproductive Factors in Nonsmokers

The authors examined hormonal factors in relation to lung cancer risk in the prospective Shanghai Women's Health Study, which recruited Chinese women aged 40 to 70 years from selected urban communities between 1996 and 2000. This analysis included 71,314 women and 220 lung cancer cases who were lifetime nonsmokers and had no history of cancer at baseline. Later age at menopause (≥ 51 vs. < 46 years; hazard ratio [HR] = 0.63), longer reproductive period (≥ 36 vs. < 31 years; HR = 0.60), higher parity (≥ 4 vs. 0 children; HR = 0.42), and intrauterine device use (HR = 0.59) were associated with decreased risks, suggesting a role for hormonal factors in the etiology of lung cancer among nonsmoking women. **(Weiss JM, Lacey JV Jr, Shu XO, Ji BT, Hou L, Yang G, Li H, Rothman N, Blair A, Gao YT, Chow WH, Zheng W. Menstrual and reproductive factors in association with lung cancer in female lifetime nonsmokers. *Am J Epidemiol* 2008;168:1319–1325)**

Changing Risks with Portable Stove Use

Domestic fuel combustion from cooking and heating, to which about 3 billion people worldwide are exposed, is associated with increased lung cancer risk. Lung cancer incidence in Xuanwei is the highest in China, and the attributable risk of lung cancer from unvented smoky coal burning is greater than 90%. To evaluate lung cancer trends after changing from unvented to portable stoves, lifetime smoky coal users in a retrospective cohort of all farmers born between 1917 and 1951 and residing in Xuanwei in 1976 were studied. Of the 42,422 enrolled farmers, 4,054 lifetime smoky coal users changed to portable stoves, 4,364 did not change, and 1,074 died of lung cancer. Portable stoves were associated with decreased risk of lung cancer mortality in men (HR = 0.62) and women (HR = 0.41), providing evidence for a cost-effective intervention that could substantially improve health in developing countries (see figure 2). **(Hosgood HD III, Chapman R, Shen M, Blair A,**

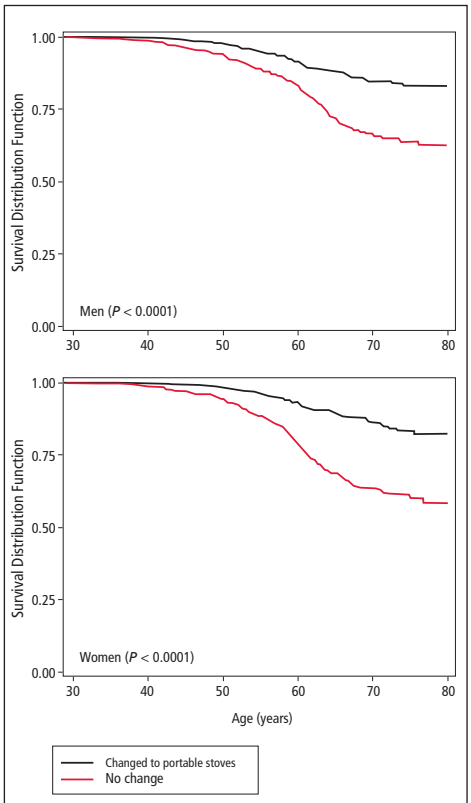


Figure 2. Survival curves for probability of lung cancer mortality for those who changed to a portable stove compared to those with no change. (Hosgood HD III, et al. 2008)

Chen E, Zheng T, Lee K-M, He X, Lan Q. Portable stove use is associated with lower lung cancer mortality risk in lifetime smoky coal users. *Br J Cancer* 2008;99:1934–1939)

Risk after Detection of Lung Scarring

A total of 66,863 cancer-free trial participants in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, aged 55 to 74 years, who received a baseline chest radiograph and were followed for up to 12 years were included in a study of localized pulmonary scarring and lung cancer risk. Scarring was present on the baseline chest radiograph for 5,041 subjects (7.5%) and was associated with elevated lung cancer risk (809 lung cancer cases; HR = 1.5). This association was specific for cancer in the lung ipsilateral to the scar (HR = 1.8) and absent for contralateral cancer (HR = 0.9). Ipsilateral lung cancer risk was elevated throughout the follow-up period (interval-specific HRs = 1.6, 2.0, 2.1, and 1.7 during 0.01–2.00, 2.01–4.00, 4.01–6.00, and 6.01–12.00 years after baseline chest radiography, respectively). Findings are consistent with the hypothesis that localized inflammatory processes associated with scarring promote the subsequent development of lung cancer. **(Yu YY, Pinsky PF, Caporaso NE, Chatterjee N, Baumgarten M, Langenberg P, Furuno JP, Lan Q, Engels EA. Lung cancer risk following detection of pulmonary scarring by chest radiography in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Arch Intern Med* 2008;168:2326–2332)**

LYMPHOMA

Etiologic Differences among NHL Subtypes

The authors present a comparison of risks for a range of putative risk factors in a population-based case-control study by lymphoma subtype, including diffuse large B-cell (DLBCL; n = 416), follicular (n = 318), and marginal zone lymphomas (n = 106) and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; n = 133). Late birth order and high body mass index ($\geq$ 35 kg/m^2) increased risk for DLBCL alone. Autoimmune conditions increased risk for marginal zone lymphoma alone. The tumor necrosis factor G-308A polymorphism (rs1800629) increased risks for both DLBCL and marginal zone lymphoma. Exposure to certain dietary heterocyclic amines from meat consumption increased risk for CLL/SLL alone. No significant risk factors for follicular lymphoma alone were observed. Data support both etiologic commonality and heterogeneity for lymphoma subtypes, suggesting that immune dysfunction is of greater etiologic importance for DLBCL and marginal zone lymphoma than for CLL/SLL and follicular lymphoma. **(Morton LM, Wang SS, Cozen W, Linet MS, Chatterjee N, Davis S, Severson RK, Colt JS, Vasef MA, Rothman N, Blair A, Bernstein L, Cross AJ, De Roos AJ, Engels EA, Hein DW, Hill DA, Kelemen LE, Lim U, Lynch CF, Schenk M, Wacholder S, Ward MH, Zahm SH, Chanock SJ, Cerhan JR, Hartge P. Etiologic heterogeneity among non-Hodgkin lymphoma subtypes. *Blood* 2008;112:5150–5160)**

Mitochondrial DNA Copy Number and NHL

Whether higher mitochondrial DNA (mtDNA) copy number in peripheral white blood cell DNA from healthy subjects is associated with later risk of NHL was examined among 104 incident male NHL cases and 104 matched controls within the prospective Alpha-tocopherol, Beta-carotene (ATBC) Cancer Prevention cohort. There was a dose-response relationship between tertiles of mtDNA copy number and risk of NHL (OR = 1.0, 1.4, and 2.4, respectively). The effect was most pronounced for the CLL/SLL subtype (OR = 1.0, 3.2, and 14.1, respectively). **(Lan Q, Lim U, Liu CS, Weinstein SJ, Chanock S, Bonner MR, Virtamo J, Albanes D, Rothman N. A prospective study of mitochondrial DNA copy number and risk of non-Hodgkin lymphoma. *Blood* 2008;112:4247–4249)**

METHODS

Combining Family and Case-control Studies

To improve power to detect genetic associations, two approaches were proposed for combining data from a case-control study and a family study that collected families with multiple cases from the same population. In the first approach, a family is viewed as the sampling unit and the joint likelihood is specified for family members using a two-level mixed-effects model to account for random familial effects and residual genetic correlations among family members. The ascertainment of the families is accommodated by conditioning on the ascertainment event. The individuals in the case-control study are treated as families of size one, and their unconditional likelihood is combined with the conditional likelihood for the families. This approach yields subject-specific maximum likelihood estimates of covariate effects. In the second approach, an individual is viewed as the sampling unit. The sampling scheme is accommodated using two-phase sampling techniques, marginal covariate effects are estimated, and correlations among family members are accounted for in the variance calculations. The models are compared in simulations. Data from studies in northeastern Italy on melanoma and a low-risk melanoma susceptibility gene, *MC1R,* are used to illustrate the approaches. **(Pfeiffer RM, Pee D, Landi MT. On combining family and case-control studies. *Genet Epidemiol* 2008;32:638–646)**

Gene-environment Interaction Tests

The authors compare four methods for testing for non-multiplicative gene-environment effects on disease risk in case-control studies: 1) the standard case-control method; 2) the case-only method, requiring an assumption of gene-environment independence; 3) a two-step method that decides between the case-only and case-control

estimators depending on a test for the gene-environment independence assumption; and 4) a novel empirical-Bayes (EB) method that combines the case-control and case-only estimators, depending on the sample size and strength of the gene-environment association in the data. The EB procedure, unlike the case-only or two-step methods, can closely maintain a desired type I error under realistic scenarios of gene-environment dependence and yet be more powerful than the traditional case-control analysis when the independence assumption is satisfied at least approximately. Analyses also reveal potential utility of some non-traditional case-control designs that sample controls at a lower rate than the cases. **(Mukherjee B, Ahn J, Gruber SB, Rennert G, Moreno V, Chatterjee N. Tests for gene-environment interaction from case-control data: A novel study of type I error, power and designs. *Genet Epidemiol* 2008;32:615–626)**

Urinary Estrogen and Metabolite Measurements

A high-performance liquid chromatography–tandem mass spectrometry method was developed to simultaneously quantitate 15 urinary estrogens and estrogen metabolites (EM): estrone; estradiol; 3 catechol estrogens; 5 estrogens in the 16α pathway, including estriol; and 5 methoxy estrogens. For a reproducibility study, two blinded, randomized aliquots from overnight urines from five follicular and five luteal premenopausal women, five naturally postmenopausal women, and five men were assayed in each of four batches. Data from 25 other participants were added to compare EM levels by menstrual/sex group and assess interindividual variability. For each EM, overall coefficients of variation were 10% or lower. Intraclass correlation coefficients for each menstrual/sex group were generally 98% or higher. Although geometric mean EM concentrations differed among the four groups, rankings were similar, with estriol, 2-hydroxyestrone, estrone, estradiol, and 16-ketoestradiol accounting for 60% to 75% of total urinary EM. Within each group, interindividual differences in absolute concentrations were consistently high; the range was 10- to 100-fold for nearly all EM. The method for measuring 15 urinary EM is highly reproducible, and the range of EM concentrations in each menstrual/sex group is quite large relative to assay variability. **(Falk RT, Xu X, Keefer L, Veenstra TD, Ziegler RG. A liquid chromatography-mass spectrometry method for the simultaneous measurement of 15 urinary estrogens and estrogen metabolites: Assay reproducibility and interindividual variability. *Cancer Epidemiol Biomarkers Prev* 2008;17:3411–3418)**

PANCREATIC CANCER

Role of Adiponectin Concentrations

The authors conducted a nested case-control study in the ATBC Cancer Prevention Study cohort of male Finnish smokers aged 50 to 69 years at baseline to test whether prediagnostic adiponectin concentrations are associated with pancreatic cancer. Among 311 exocrine pancreatic cancer cases diagnosed between January 1985 and October 2004 and 510 controls, higher adiponectin concentrations were inversely associated with pancreatic cancer (for highest [> 9.8 μ/ml] vs. lowest quintile [≤ 4.6 μ/ml], OR = 0.65; p for trend = 0.04). The inverse association was significant among cases diagnosed five or more years after blood collection (n = 238; for highest vs. lowest quintile, OR = 0.55). **(Stolzenberg-Solomon RZ, Weinstein S, Pollak M, Tao Y, Taylor PR, Virtamo J, Albanes D. Prediagnostic adiponectin concentrations and pancreatic cancer risk in male smokers. *Am J Epidemiol* 2008;168:1047–1055)**

PROSTATE AND COLON CANCER

Resequencing a Region of Chromosome 8q24

At least three regions of chromosome 8q24 have been independently associated with prostate cancer risk. Haplotypes in two contiguous but independent loci, marked by rs6983267 and rs1447295, were identified in the Cancer Genetic Markers of Susceptibility project (http://cgems.cancer.gov), which genotyped more than 5,000 prostate cancer cases and controls of European origin. The rs6983267 locus is also strongly associated with colorectal cancer. To ascertain a comprehensive catalog of common SNPs across the two regions, the authors conducted a resequence analysis of 136 kb (chr8: 128,473,000–128,609,802) using the Roche/454 next-generation sequencing technology in 39 prostate cancer cases and 40 controls of European origin. They characterized a comprehensive catalog of common SNPs within this region, including 442 novel SNPs, and have determined the pattern of linkage disequilibrium. Results should be useful for choosing SNPs for fine mapping of association signals in 8q24 and investigations of the functional consequences of select common variants. **(Yeager M, Xiao N, Hayes RB, Bouffard P, Desany B, Burdett L, Orr N, Matthews C, Qi L, Crenshaw A, Markovic Z, Fredrikson KM, Jacobs KB, Amundadottir L, Jarvie TP, Hunter DJ, Hoover R, Thomas G, Harkins TT, Chanock SJ. Comprehensive resequence analysis of a 136 kb region of human chromosome 8q24 associated with prostate and colon cancers. *Hum Genet* 2008;124:161–170)**

RADIATION

Chromosome Translocations in Technologists

Radiologic technologists were surveyed to determine whether their personal cumulative exposure to diagnostic x-rays was associated with increased frequencies of chromosome translocations, an established radiation biomarker possibly suggesting increased cancer risk. Within a large cohort of U.S. radiologic technologists, 150 provided a blood sample for whole-chromosome painting and were interviewed about past x-ray examinations. The number and

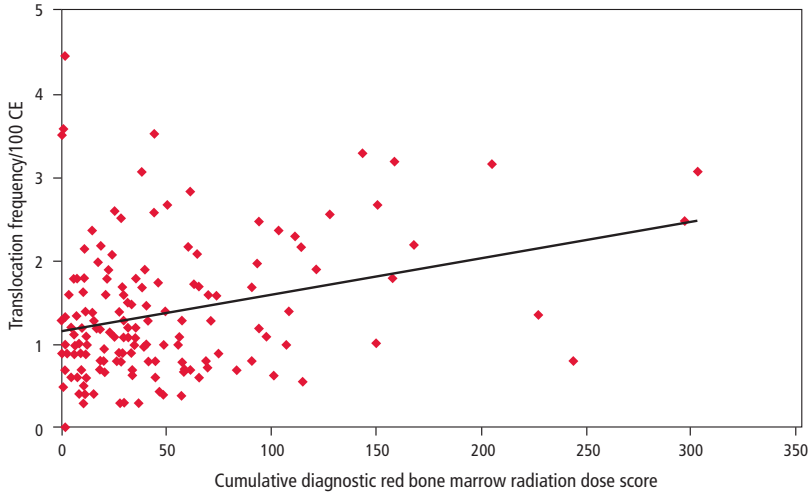


Figure 3. Translocation frequency versus the cumulative diagnostic RBM radiation dose score among 150 U.S. radiologic technologists. (Sigurdson AJ, et al. 2008)

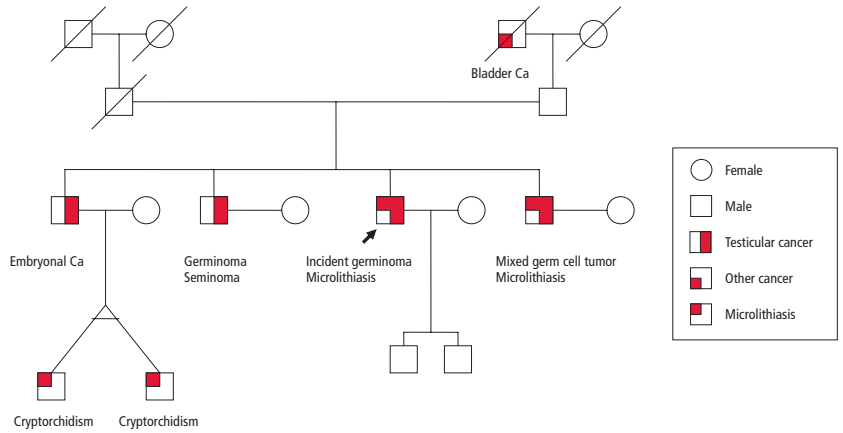


Figure 4. Family pedigree showing four brothers with testicular cancer, two of whom have testicular microlithiasis. (Korde LA, et al. 2008)

types of examinations reported were converted to a red bone marrow (RBM) dose score with units that approximated 1 mGy. The estimated mean cumulative RBM radiation dose score was 49 (range = 0–303). After adjustment for age, translocation frequencies significantly increased with increasing RBM dose score with an estimate of 0.004 translocations per 100 cell equivalents per score unit (see figure 3). The slope estimate was consistent with expectations based on cytogenetic experience and atomic bomb survivor data. **(Sigurdson AJ, Bhatti P, Preston DL, Doody MM, Kampa D, Alexander BH, Petibone D, Yong LC, Edwards AA, Ron E, Tucker JD. Routine diagnostic X-ray examinations and increased frequency of chromosome translocations among U.S. radiologic technologists. *Cancer Res* 2008;68:8825–8831)**

SMALL INTESTINAL CANCER

Dietary Factors

Meat and fat intakes were investigated in relation to small intestinal cancer among a half million men and women enrolled in the NIH-AARP Diet and Health Study. During up to eight years of follow-up, 60 adenocarcinomas and 80 carcinoid tumors of the small intestine were diagnosed. Despite slightly elevated HRs for red meat, there were no clear associations of red or processed meat intake with either adenocarcinoma or carcinoid tumors of the small intestine. In contrast, the authors noted a markedly elevated risk for carcinoid tumors of the small intestine with saturated fat intake in both categorical (highest vs. lowest tertile: HR = 3.18) and continuous data (HR = 3.72 for each 10g increase in intake per 1,000 kcal). Positive associations for meat intake reported in previous case-control studies may be partly explained by saturated fat intake. **(Cross AJ, Leitzmann MF, Subar AF, Thompson FE, Hollenbeck AR, Schatzkin A. A prospective study of meat and fat intake in relation to small intestinal cancer. *Cancer Res* 2008;68:9274–9279)**

TESTICULAR CANCER

Microlithiasis in Familial Cases and Relatives

A total of 48 men affected with familial testicular germ cell tumors (FTGCT) and 33 unaffected men from 31 families with at least two testicular cancer cases underwent testicular ultrasound (see figure 4). Testicular microlithiasis (TM) was more prevalent among FTGCT family members than described previously in the general population and was more frequent in the contralateral testicles of affected men than unaffected men (48% vs. 24%). The association appeared stronger for classic TM (≥ 5 microliths, 21% vs. 9%) than for limited TM (< 5 microliths, 27% vs. 15%). TM was bilateral in six of seven (87%) unaffected men. Among affected men, TM was not associated with histology, age at diagnosis, or cancer treatment. Of the 31 families, 10 accounted for a majority (61%) of the TM cases identified (p = 0.11). Findings suggest both a familial predisposition to TM and an association between TM and FTGCT. **(Korde LA, Premkumar A, Mueller C, Rosenberg P, Soho C, Bratslavsky G, Greene MH. Increased prevalence of testicular microlithiasis in men with familial testicular cancer and their relatives. *Br J Cancer* 2008;99:1748–1753)**

DCEG PEOPLE IN THE NEWS

In October, **Michael C.R. Alavanja, Dr.P.H., Laura Beane-Freeman, Ph.D., Kenneth P. Cantor, Ph.D., M.P.H.,** and **Mary H. Ward, Ph.D.,** all of the Occupational and Environmental Epidemiology Branch (OEEB), gave presentations at the President's Cancer Panel meeting on Environmental Factors in Cancer: Agricultural Exposures, held in Indianapolis.

This fall, **Blanche P. Alter, M.D., M.P.H.,** Clinical Genetics Branch (CGB), gave talks on inherited bone marrow failure syndromes at Johannesburg General Hospital in South Africa; the University of Texas M.D. Anderson Cancer Center and Baylor College of Medicine in Houston; Johns Hopkins School of Medicine in Baltimore; Howard University School of Medicine in Washington, DC; Driscoll Children's Hospital in Corpus Christi, Texas; the Twentieth Annual Fanconi Anemia Research Fund Scientific Symposium in Eugene, Oregon; and the Keck Center of the National Academies in Washington, DC.

In October, Dr. Beane-Freeman and **Lee E. Moore, Ph.D.** (OEEB), gave invited lectures on biomarker and genetic-based research at the Barcelona workshop, Getting Unstuck in Environmental and Occupational Cancer, sponsored by the Centre for Research in Environmental Epidemiology.

Amy Berrington de Gonzalez, D.Phil., Radiation Epidemiology Branch, gave an invited lecture on "Second cancers after radiotherapy for breast cancer in SEER and the UK Million Women Study" at Oxford University in August and at the Memorial Sloan-Kettering Cancer Center in November.

In November, **Philip E. Castle, Ph.D., M.P.H.,** Hormonal and Reproductive Epidemiology Branch (HREB), gave invited talks on "New biomarkers for detection of cervical precancer and cancer," "Risk assessment of cervical cancer: Practical issues," and "Self-collection and HPV testing" at the Eurogin 2008 Conference in Nice, France, titled Joining Forces for Cervical Cancer Prevention.

In September, **Amanda J. Cross, Ph.D.,** Nutritional Epidemiology Branch (NEB), spoke on "Meat intake and colorectal cancer: Recent research activities related to carcinogens in meat" at the Gene-environment Interactions for Colorectal Cancer meeting at Lincoln University in Pennsylvania.

In September, **James J. Goedert, M.D.,** Infections and Immunoepidemiology Branch (IIB), gave a talk on "Cancer incidence and risk factors with HIV/AIDS: An update" at the Third Workshop on Complications of HIV and Antiretroviral Treatments in Avignon, France.

In September, **Mark H. Greene, M.D.** (CGB), spoke on "Familial testicular germ cell tumors in adults: Summary of current genetic and clinical phenotype data" at the 11th International Workshop on Multiple Endocrine Neoplasia in Delphi, Greece. In November, he presented "Update on recent developments in the management of patients with BRCA1/2 mutations" at the 24th Annual Ella T. Grasso Memorial Conference at the Yale School of Medicine.

In October, **Wen-Yi Huang, Ph.D., M.S.P.H.** (OEEB), cochaired the colorectal cancer session and presented "Ongoing research findings from the Prostate, Lung, Colorectal, and Ovarian screening trial on etiology of colorectal tumors" at the Eighth International Conference of Anticancer Research in Kos, Greece.

In November, **Li Jiao, M.D., Ph.D.** (NEB), spoke on "Genes, diet, and risk of pancreatic cancer" at the Albert Einstein College of Medicine in New York.

In November, **Hormuzd A. Katki, Ph.D.,** Biostatistics Branch (BB), spoke on "Using DNA fingerprints to infer familial relationships within NHANES-III households" at the National Human Genome Research

KELLY BOLTON RECEIVES NICK DAY PRIZE

Kelly Bolton, Hormonal and Reproductive Epidemiology Branch, an NIH-Oxford-Cambridge Scholars Program Fellow, completed requirements for her M.Phil. degree in epidemiology from the University of Cambridge, United Kingdom, where she was also the joint winner of the Nick Day Prize for the best M.Phil. student in the epidemiology program. Her master's thesis is titled "Ovarian cancer prognosis: A genome-wide association study." Her mentors are **Montserrat García-Closas, M.D., Dr.P.H.,** and Dr. Paul D.P. Pharoah of the University of Cambridge.

Kelly Bolton receives award from Nicholas Day, former head of the Department of Public Health and Primary Care at Cambridge.

Institute. In December, he gave a talk titled "Introduction to options for design and analysis of studies nested within cohorts" at the Center on Aging and Health at Johns Hopkins University.

In December, **Jill Koshiol, Ph.D.** (IIB), won a Scholar-in-Training Award from the American Association for Cancer Research at the International Conference on Infection and Cancer: Biology, Therapeutics, and Prevention, held in Hong Kong.

In October, **James V. Lacey, Jr., Ph.D.** (HREB), spoke on "PTEN as a marker of clinical progression from endometrial hyperplasia to carcinoma" at the Fifth Annual Uterine Cancer Biology Symposium at the Memorial Sloan-Kettering Cancer Center in New York.

In December, **Maria Teresa Landi, M.D., Ph.D.,** Genetic Epidemiology Branch (GEB), spoke on "MicroRNA expression: Lung cancer" at NIH Clinical Center Grand Rounds.

In October, **Mary Lou McMaster, M.D.** (GEB), gave a talk on "Precursor conditions in Waldenstrom macroglobulinemia" as part of the invited faculty at the Fifth International Workshop on Waldenstrom's Macroglobulinemia in Stockholm.

Roberto Minutillo has been selected as the new DCEG Deputy Administrative Resource Center (ARC) manager. He began his career with the ARC as an intern in 1998 and became an administrative officer in 1999. In 2007 he left the ARC to accept a promotion to senior administrative officer at the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Later that year he returned to the ARC as a lead administrative officer, where he oversaw the administrative operations for the Laboratory of Translational Genomics and the Core Genotyping Facility. With his wealth of experience in all areas of administration, he will continue to be a great resource to the Division.

In October, **Lisa Mirabello, Ph.D.** (CGB), presented a poster on "Worldwide genetic structure in 37 genes important for telomere maintenance using Human Genome Diversity Project data" at the annual meeting of the American Society of Human Genetics (ASHG).

At the ASHG meeting, **Christine Mueller, D.O.** (CGB), gave an invited platform talk titled "Detailed characterization of the dyskeratosis congenita phenotypic spectrum."

In October, **Ruth M. Pfeiffer, Ph.D.** (BB), gave a talk titled "A colorectal cancer risk prediction tool" at a biostatistics seminar at Massachusetts General Hospital in Boston.

In December, **Philip R. Taylor, M.D., Sc.D.** (GEB), taught "Chemoprevention of cancer" at the Fundamentals of Clinical Oncology for Public Health Practitioners course at Johns Hopkins University.

Dr. Ward and **Aaron E. Blair, Ph.D., M.P.H.** (OEEB), gave invited presentations at the Canadian Cancer Society's meeting, Exploring the Connection: A State of the Science Conference on Pesticides and Cancer. Dr. Ward spoke on "Non-occupational pesticides and cancer," and Dr. Blair presented "Occupational pesticide exposures and cancer."

In November, **Stephanie J. Weinstein, Ph.D.** (NEB), presented "The Rare Cancers Vitamin D Pooling Project" at the 2008 annual meeting of the NCI Cohort Consortium in Bethesda.

At the Eurogin 2008 Conference in Nice, **Nicolas Wentzensen, M.D., Ph.D.** (HREB), chaired a session on molecular markers and spoke on "HPV genotype distribution among 1,700 women referred to colposcopy: Implications for disease classification and type attribution." In October, Dr. Wentzensen gave an invited presentation on "How to improve the accuracy of the gold standard to ascertain presence of cervical cancer precursors?" at the 16th Cochrane Colloquium in Freiburg, Germany.

With mentors Dr. Elizabeth Platz (Johns Hopkins Bloomberg School of Public Health) and Dr. García-Closas, **Hannah P. Yang, Sc.M.** (HREB), successfully defended her doctoral dissertation on "The association of smoking and common variants in estrogen metabolizing genes with endometrial cancer risk" in the Polish Endometrial Cancer Study and was recommended for a Ph.D. in epidemiology. She will remain in HREB during her postdoctoral training.

In October, **Rose Yang, Ph.D., M.P.H.** (GEB), gave an invited talk at the workshop Radiation Risk of Breast Cancer: What Can and Should We Do in the Future? sponsored by the Radiation Effects Research Foundation and the National Institute of Radiological Sciences in Hiroshima.

Kai Yu, Ph.D. (BB), spoke on "Population substructure and control selection in genome-wide association studies" at the Department of Biostatistics and Epidemiology at the University of Pennsylvania in September and at the Department of Epidemiology at the University of Texas M.D. Anderson Cancer Center in October. That same month, he also gave a talk on "A partially linear tree-based regression model for multivariate outcomes" at the Texas A&M University Department of Statistics.

COMINGS . . . GOINGS


Laufey Amundadottir

Laufey Amundadottir, Ph.D., has joined the Laboratory of Translational Genomics as a tenure-track investigator. She received her doctoral degree from Georgetown University and completed her postdoctoral training at Harvard Medical School before joining deCODE genetics in Iceland as the head of the Division of Cancer Genetics, where she conducted linkage and association analyses in multiple cancers. Her main interest is investigating the genetics and biology of cancers, including pancreatic and prostate cancer. Her laboratory focuses on identifying and characterizing causal genetic variants discovered through genome-wide association studies and on better understanding the role of common sequence variation in the development of cancer.


Carrie Daniel

Carrie R. Daniel, Ph.D., M.P.H., has joined the Nutritional Epidemiology Branch (NEB) as a postdoctoral fellow. She received a master's degree in epidemiology and a doctoral degree in nutrition from Emory University. She conducted her research and training in cancer and nutritional epidemiology with Dr. Robin Bostick at Emory University and Dr. Marji McCullough at the American Cancer Society (ACS). Her translational research background includes work at the Arizona Health Sciences Center, CDC, Emory Winship Cancer Institute, and ACS. With her mentor, **Rashmi Sinha, Ph.D.,** Dr. Daniel is investigating diet and nutrition in the etiology of renal cancer and non-Hodgkin lymphoma and is involved in methodological considerations for the Indian Health Study.

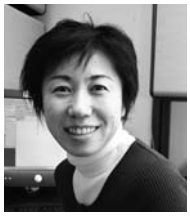

Samantha Jordan

Samantha Jordan has joined NEB as a Howard Hughes Medical Institute-NIH Research Scholars Fellow. She holds a B.S. in biochemistry from Tufts University and is currently a doctoral student at Tufts University School of Dental Medicine. She is working with **Christian C. Abnet, Ph.D., M.P.H.,** and **Yikyung Park, Sc.D.,** on the association between tooth loss and cancer risk as well as other studies.

In October, **Jill Koshiol, Ph.D.,** joined the Infections and Immunoepidemiology Branch as a research fellow. She previously worked in the Genetic Epidemiology Branch (GEB). She is continuing her research on the role of human papillomavirus in the etiology of non-cervical cancer as well as infections associated with lung and hematopoietic malignancies.

Ola Landgren, M.D., Ph.D. (GEB), has transferred to the Center for Cancer Research (CCR) to pursue his clinical interests. He joined GEB as a visiting fellow in 2004 and became a tenure-track investigator in 2006. While in DCEG, he investigated the etiology of hematopoietic malignancies and lymphoproliferative disorders, including the relation of monoclonal gammopathy of undetermined significance to multiple myeloma. He will continue to collaborate with DCEG investigators as he establishes his new research portfolio in CCR.

In January, **Christine Mueller, D.O.,** left the Clinical Genetics Branch to take a position as a clinical reviewer of therapies for inborn errors of metabolism at the U.S. Food and Drug Administration.


Ritsu Sakata

Ritsu Sakata, Ph.D., of the Radiation Effects Research Foundation (RERF) in Hiroshima, Japan, has joined the Radiation Epidemiology Branch as a special volunteer for six months. She is working with **Kiyohiko Mabuchi, M.D., Dr.P.H.,** and **Peter D. Inskip, Sc.D.,** on studies of radiation-related cancer risk in a cohort of women who were previously irradiated for treatment of benign gynecological diseases. She replaces **Kyoji Furukawa, Ph.D.,** who will be returning to RERF to continue his research on radiation risk estimates for cancer in the cohort of atomic bomb survivors in Hiroshima and Nagasaki.


Laura Sue

In July, **Laura Sue, M.P.H.,** joined the Epidemiology and Biostatistics Program as a Cancer Research Training Award Fellow after completing her master's degree at the Yale School of Public Health. She is working with **Regina G. Ziegler, Ph.D., M.P.H.,** on projects related to anthropometry, estrogens and estrogen metabolism, and breast cancer risk.

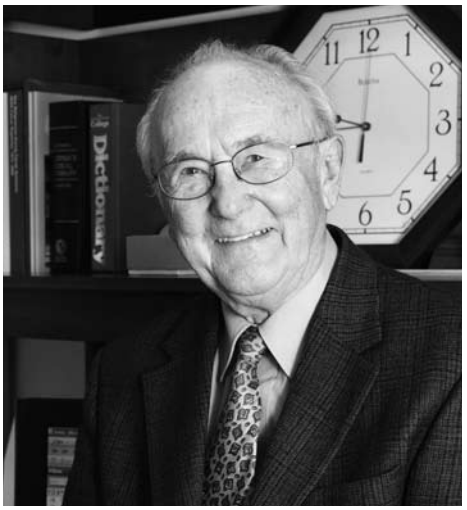
IHOR MASNYK RETIRES

Ihor J. Masnyk, Ph.D., Radiation Epidemiology Branch (REB), retired in December after a 46-year career at NCI. Born in Ukraine in 1930, Dr. Masnyk grew up in the midst of World War II and came to the United States as an adolescent after spending time in displaced person camps in Czechoslovakia and Germany, experiences that left him with great strength and resolve. He earned a Ph.D. in organic chemistry from the University of Chicago, a task he accomplished while in the U.S. Army active duty service and later the Retired Reserve, where he earned the rank of Colonel.

In 1962, Dr. Masnyk joined NCI as a chemist in the Endocrine Evaluation Branch. His career at NCI included positions as Chief of the Planning and Analysis Branch and Director of the Extramural Research Program, Division of Cancer Biology and Diagnosis (DCBD); Acting Associate Director for the Office of International Affairs; and Deputy Director of the Division of Cancer Biology, Diagnosis, and Centers.

NCI Deputy Director Dr. Alan S. Rabson recalls, "Ihor was the perfect person to manage the extramural programs of DCBD. I worked with him for many years, and we had a wonderful and warm working and personal relationship. Ihor was an extremely knowledgeable chemist and yet he was able to transform himself into a skilled program manager."

In 1995, Dr. Masnyk began working with the Radiation Effects Branch in the Division of Cancer Biology to design and implement the NCI Chornobyl research program, which was later transferred to DCEG. His chemistry background, language skills, dedication, and creative thinking as project director were instrumental in the success of this complex program, which included study populations in Ukraine and Belarus. He was adept in managing the diplomatic, financial, purchasing, and contractual aspects of the program and in serving as a translator and guide to the culture and traditions of Ukraine and Belarus.



Ihor Masnyk

Dr. Masnyk is an accomplished musician who plays ancient instruments and leads his church choir. He is also a master craftsman of traditional Easter eggs and a fine ballroom dancer. During his retirement, he will pursue these interests and others and spend time with friends and family. Fortunately for NCI, he will continue to consult with REB staff to guarantee the smooth completion of the Chornobyl projects. ■

—Maureen C. Hatch, Ph.D.,
and Elaine Ron, Ph.D., M.P.H.

NIH Publication No. 09-6051
Printed March 2009