National Cancer Institute

DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS

Linkage

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IN THIS ISSUE:

Obesity: A Provocative Question and the Search for Answers

NCI Director Harold Varmus, M.D., created the "Provocative Questions" initiative to assemble a list of important topics and advances that will stimulate NCI's research communities to use laboratory, clinical, and population sciences in effective and imaginative ways. One question particularly resonates for DCEG investigators: What molecular mechanisms underlie the association of obesity with the risks of cancer?

Obesity has become a major public health problem in the United States and elsewhere in the world, affecting rates of cardiovascular disease, endocrine disorders such as diabetes, and cancer. Many studies have documented the contribution of obesity to the incidence of (and death from) a number of cancers, including colon, breast (in postmenopausal women), endometrium, kidney, esophagus (adenocarcinoma), gastric cardia, pancreas, gallbladder, and liver. How this happens—what the mechanisms are that underpin these associations—is poorly understood.

Obesity is not a singular condition that affects our health, and many factors modify its effects. These factors include *age*—when a person first becomes obese and for how long; *physical activity*—how much and how often we move around; and our *ethnic/racial makeup*—which can affect the way we gain and maintain weight. Furthermore, specific biomarkers may mediate the obesity-cancer links, such as hormones and a range of metabolites (i.e., the substances left when the body breaks down food, drugs, or other chemicals). Thus, understanding obesity's role in cancer requires a multifaceted research approach.

Apple and pear body shapes are often used to describe variations in fat storage.

Cancer Sites

DCEG investigators are conducting wide-ranging research on obesity and cancer risks. Emerging technologies, such as high-throughput assays and the large-scale collection and storage of biospecimens, have been especially helpful in allowing

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Joseph F. Fraumeni, Jr., Director
Shelia Hoar Zahm, Deputy Director

Managing Editor
Wendy Schneider-Levinson (schneiderleviw@mail.nih.gov)

Editor
Victoria A. McCallum (mccallumva@mail.nih.gov)

Scientific Highlights
Editor – *Patricia Madigan* (madiganp@mail.nih.gov)
Graphics – *David P. Check* (checkd@mail.nih.gov)

DCEG Linkage **Reporters**
Epidemiology and Biostatistics Program
Sarah Del Castillo (delcastillos@mail.nih.gov)
Biostatistics Branch
Prisca Fall-Keita (fallpn@mail.nih.gov)
Clinical Genetics Branch
June A. Peters (petersju@mail.nih.gov)
Genetic Epidemiology Branch
Barbara Rogers (rogersb2@mail.nih.gov)
Hormonal and Reproductive Epidemiology Branch
Patricia Madigan (madiganp@mail.nih.gov)
Infections and Immunoepidemiology Branch
Cindy Chang (changcm@mail.nih.gov)
Laboratory of Translational Genomics
Tammy Bell (bellta@mail.nih.gov)
Nutritional Epidemiology Branch
Alison Mondul (mondulam@mail.nih.gov)
Occupational and Environmental Epidemiology Branch
Gabriela Cadena (cadenag@mail.nih.gov)
Radiation Epidemiology Branch
Jenna Nober (noberj@mail.nih.gov)
DCEG Committee of Scientists
Christian C. Abnet (abnetc@mail.nih.gov)
DCEG Representatives to the NIH Women Scientists Advisory Group
Patricia Hartge (hartgep@mail.nih.gov)
Mary Ward (wardm@mail.nih.gov)
DCEG Representative to the NIH Tenure-track Investigators Committee
Sam M. Mbulaiteye (mbulaits@mail.nih.gov)
DCEG Representatives to the NIH Staff Scientists/Staff Clinicians Organization
Gabriella Andreotti (andreotg@mail.nih.gov)
Amanda Black (blacka@mail.nih.gov)
DCEG Representatives to the NIH Fellows Committee
Phoebe Lee (leeps@mail.nih.gov)
Alison Mondul (mondulam@mail.nih.gov)

Palladian Partners, Inc.
Elaine Garber (egarber@palladianpartners.com)

investigators to examine these relationships as never before. Endometrial cancer draws attention because it shows one of the strongest relationships to obesity of all the cancers. **Louise A. Brinton, Ph.D.,** Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), Dr. Mia M. Gaudet of the American Cancer Society (a former fellow in HREB), **Mark E. Sherman, M.D.** (HREB), and colleagues are using high-throughput technologies for a metabolomic assessment of body mass index (BMI) and the risk of endometrial cancer in DCEG's Polish Women's Health Study. From a panel of 69 study metabolites (including 15 amino acids, 45 acylcarnitines, and 9 fatty acids), the investigators discovered 7 metabolites significantly associated with the risk of endometrial cancer, even when adjusting for BMI. "This study provides the first evidence that metabolomic profiles in serum can be used to disentangle the biologic mechanisms that influence this obesity-related cancer," said senior author Dr. Sherman.

The incidence of esophageal adenocarcinoma (EAC), another obesity-related cancer, has been rising more rapidly than any other cancer in the United States. Scientists have hypothesized that obesity causes a mechanical change in esophageal sphincter tone, which allows gastroesophageal reflux, a known risk factor for EAC. A recent investigation by **Christian C. Abnet, Ph.D., M.P.H.,** Nutritional Epidemiology Branch (NEB), within the NIH-AARP Diet and Health Study of more than 500,000 subjects, found that individuals with high levels of obesity have a significantly increased risk of EAC compared with people whose weight falls within the normal range. Dr. Abnet and colleagues also are investigating whether body shape and fat distribution are independently associated with risk for EAC and gastric cardia adenocarcinoma. So far, the data indicate an increased risk of EAC associated with both high BMI and high waist-to-hip ratio, whereas gastric cardia adenocarcinoma is associated only with high BMI.

World Health Organization (WHO) Classifications for Obesity Corresponding to Body Mass Index (BMI)

WHO Classification	BMI (kg/m²)
Underweight	< 18.50
Normal range	18.50–24.99
Overweight	25.00–29.99
Obesity class I	30.00–34.99
Obesity class II	35.00–39.99
Obesity class III	≥ 40.00

Philip R. Taylor, M.D., Sc.D., Genetic Epidemiology Branch, and colleagues are investigating biomarkers associated with Barrett's esophagus (BE), a lesion that is a precursor to EAC, in a study at the National Naval Medical Center in Bethesda, Maryland. Efforts are being made to identify biomarkers for BE diagnosis, susceptibility states, and progression to dysplasia or EAC.

The incidence of thyroid cancer also has increased significantly in the United States since the early 1980s, and until recently, the connection between obesity and thyroid cancer remained uncertain. However, **Cari Meinhold Kitahara, Ph.D.,** Radiation Epidemiology Branch (REB), and other DCEG investigators pooled data from five prospective U.S. studies comprising approximately 850,000 subjects and found that high BMI increased the risk of thyroid cancer in both men and women (see Figure 1).

The prevalence of prostate cancer, the most common cancer in men in the United States, appears to be rising around the world, but the etiologic role of obesity has remained elusive. A recent review of existing data led by **Ann W. Hsing, Ph.D.,** Infections and Immunoepidemiology Branch, revealed

an increased incidence of high-grade prostate cancer and a decreased incidence of low-grade tumors associated with obesity. In addition, prostate cancer mortality was consistently associated with obesity in several studies. Research findings have suggested that obesity may influence the risk of prostate cancer through its effects on androgen metabolism and interaction with other risk factors, such as insulin resistance, diabetes, inflammation, and genetic susceptibility.

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study cohort, **Demetrius Albanes, M.D.** (NEB), and other investigators found a strong positive association between fasting serum insulin concentrations and the risk of prostate cancer. Despite the association of diabetes with higher rates of many other cancers, **Neal D. Freedman, Ph.D., M.P.H.,** and **Gabriel Lai, Ph.D.,** both of NEB, and their colleagues recently confirmed that diabetes is associated with lower rates of incident prostate cancer. The mechanism of the association between diabetes and a decreased risk of prostate cancer may involve insulin metabolism or genetic pathways.

Cancer Mechanisms

Weight distribution may provide a clue to the mechanism by which obesity is tied to the risk of cancer. Fat located around the body's midsection may operate differently than body fat overall, and waist circumference (WC) represents a measure that accounts for the accumulation of abdominal fat. Using the NIH-AARP Diet and Health Study, Dr. Michael F. Leitzmann, formerly of NEB, **Steven C. Moore, Ph.D.** (NEB), and colleagues examined WC and BMI in relation to cause-specific death. Increased abdominal fat as measured by WC was related to a higher risk of several major causes of death, including lung cancer and chronic respiratory disease, independent of BMI (see Figure 2 on page 4).

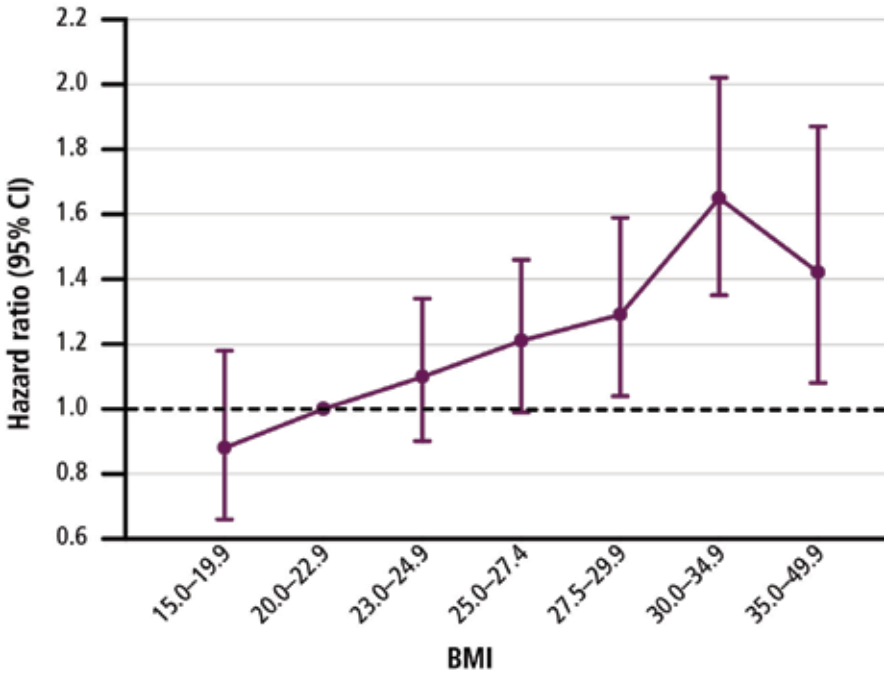


Figure 1. Estimated hazard ratios and confidence intervals (CIs) for thyroid cancer risk according to body mass index (BMI). BMI is the weight in kilograms divided by the square of the height in meters. (Kitahara CM, et al. *Cancer Epidemiol Biomarkers Prev* 2011)

Physical activity and sedentary behavior also may have differential effects on risk associated with obesity, giving clues to mechanism. Using information recorded by a lightweight accelerometer used for the National Health and Nutritional Examination Survey (NHANES) in 2003–2004, **Charles Matthews, Ph.D.** (NEB), and colleagues reported the first objective data on the amount of time spent in overall sedentary behaviors in a nationally representative sample. After adjusting for the effect of exercise, the amount of daily sedentary time was linked to levels of C-reactive protein, insulin, and other cardio-metabolic biomarkers. According to Dr. Matthews, "To understand the mechanisms linking physical activity and carcinogenesis, we have to expand our repertoire of exposure assessments so that we can look at the effects of too much sitting, not just too little exercise."

In addition, excess weight may operate differently across the life span—a special concern given the increasing prevalence of overweight and obesity among children, adolescents, and young adults each year. Current DCEG research includes a systematic investigation within the NIH-AARP Diet and Health Study, led by **Amy Berrington de González, D.Phil.** (REB), Dr. Kitahara, and Dr. Moore, that seeks to relate the risk of different forms of cancer to BMI at various ages (i.e., 18, 35, and 50 years old and age at study entry) as well as to weight gain throughout adulthood. This comprehensive study will help to identify critical time periods during which obesity influences cancer induction and progression, which might help inform more effective prevention interventions.

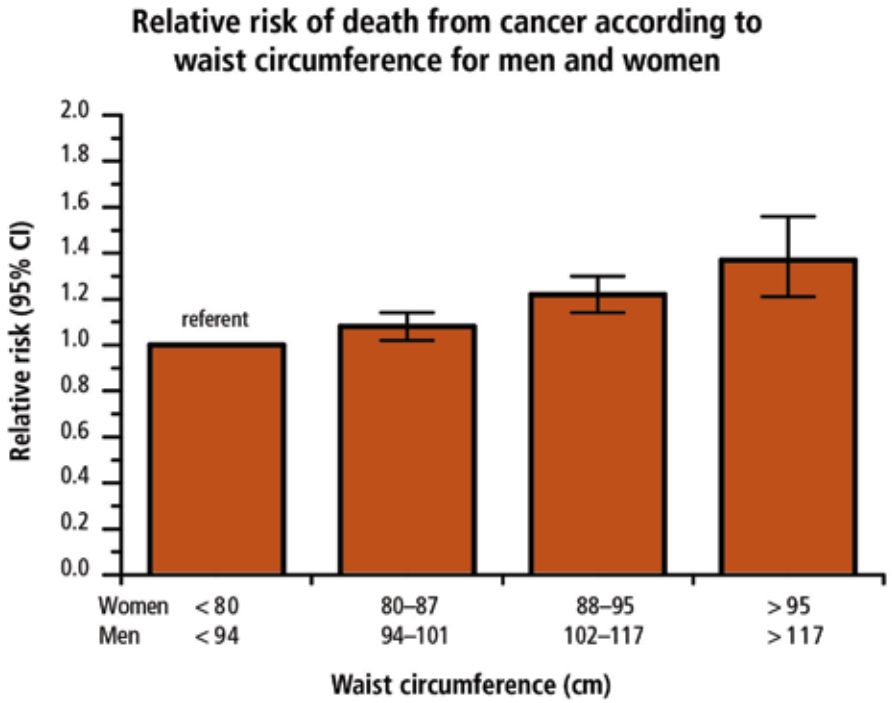


Figure 2. Relative risk of death from cancer according to waist circumference in centimeters (cm) for men and women. The analyses of waist circumference were adjusted for body mass index. CI = confidence interval. (Figure is based on Table 2 from Leitzmann MF, et al. *PLoS ONE* 2011.)

The Way Forward

Large-scale biospecimen collections are allowing molecular epidemiologists to use more advanced analyses of metabolites and other biomarkers. In addition, new tools for data collection are providing investigators with the means to think creatively and push the boundaries in linking nutrition and cancer. For example, accelerometers offer the ability to continuously record data for physical activity over specified time intervals. New web-based tools developed by DCEG and collaborators in the NCI Division of Cancer Control and Population Sciences and the Division of Cancer Prevention, such as the Physical Activities Completed over Time in 24 Hours (ACT-24) and the Automated Self-Administered 24-Hour Dietary Recall (ASA24), allow participants to enter information on physical activity or diet in a convenient, online format.

In response to the growing importance and interest in the field, NEB investigators Dr. Matthews, Dr. Moore, and Deputy Chief **Rashmi Sinha, Ph.D.,** recently established the DCEG Energy Balance and Obesity Working Group to further interdisciplinary research. Through ongoing collaborations with the NCI Cohort Consortium and other collaborative networks, the availability of state-of-the-art methods and tools is allowing DCEG investigators to contribute to the search for mechanisms underpinning the association of obesity with the risks of cancer. ■

—Victoria A. McCallum, M.P.H., and Wendy Schneider-Levinson

DCEG TRAINING PROGRAM RECEIVES LANGMUIR AWARD

In June, DCEG received the inaugural Alexander D. Langmuir Award for Training Program Excellence and Innovation. **Jackie Lavigne, Ph.D., M.P.H.,** Chief of DCEG's Office of Education (OE), accepted the award during a ceremony at the Third North American Congress of Epidemiology in Montreal, Canada.

The objectives of the award are to highlight epidemiology training programs that emphasize research experience and skills development, the application of epidemiology principles and advanced methods, and the importance of collaborative and integrative epidemiologic approaches. "This award acknowledges NCI's training program for having developed and implemented creative educational offerings that effectively train future leaders in epidemiology," said Dr. John Vena, the Award Committee Chair.

Training the next generation of scientists was the strategic focus for Division Director **Joseph F. Fraumeni, Jr., M.D.,** when he established OE in 1999. Having an office dedicated to training across the Division enables DCEG to offer its fellows the potential to work with and learn from experts in many aspects of epidemiology and genetics. Under the guidance of dedicated, experienced mentors, DCEG fellows gain in-depth experience in designing and executing research studies, analyzing data, and interpreting and publishing the results. Evidence for the success of trainees in the DCEG environment lies in their record of publishing innovative and high-quality research. Current and recent DCEG fellows are represented as lead authors in most of the top journals in the field. In addition, DCEG offers a variety of practical opportunities for fellows to develop a comprehensive set of professional skills, including giving research presentations (at local, national, and international meetings), planning scientific events, mentoring, and grant writing.

The award honors the memory of Alexander D. Langmuir, who created the Epidemic Intelligence Service, a combined training and service program for epidemiologists at what is now known as the Centers for Disease Control and Prevention in Atlanta, Georgia.

—Jackie Lavigne, Ph.D., M.P.H.

NCI COHORT CONSORTIUM INVESTIGATES THE ROLE OF OBESITY

In many developed countries today, more than half the population is overweight or obese, and the potential impact of this situation on total mortality has drawn considerable attention. In 2008, investigators from more than two dozen prospective studies in the NCI Cohort Consortium formed a collaboration to measure the mortality effects of body mass index (BMI, kg/m^2) and related factors. The initiative is led by **Patricia Hartge, Sc.D.,** Deputy Director of DCEG's Epidemiology and Biostatistics Program; Dr. Michael Thun of the American Cancer Society in Atlanta, Georgia; and Dr. Walter Willett of the Harvard School of Public Health in Boston, Massachusetts.

The first in a series of studies combined the data from 1.46 million persons of European ancestry, of which 160,087 died during a median follow-up of 10 years. Among the healthy never-smokers (i.e., no self-reported history of cancer or heart disease at baseline, deaths = 35,369), a J-shaped relationship was seen between BMI and all-cause mortality, with the lowest mortality at normal weight (BMI = 20.0–24.9). Men and women showed similar effects, which were strongest for BMI measured at younger ages and weakest for BMI measured after age 70. **Amy Berrington de González, D.Phil.,** Radiation Epidemiology Branch, lead author of the paper published about this study in the *New England Journal of Medicine,* noted, "In this study, we focused on whites living in developed countries due to their large numbers in our study populations. As the relationship between BMI and mortality may vary across racial and ethnic groups, our next priority is to study the effects of BMI on minority populations of the United States."

The African American population, in particular, warrants investigation, with 1 in 10 adults in this group now in the morbidly obese category (BMI ≥ 40). **Yikyung Park, Sc.D.,** Nutritional Epidemiology Branch (NEB), and colleagues are pursuing earlier findings from the NIH-AARP Diet and Health Study and other cohorts, which surprisingly showed that mortality rose less steeply with higher BMI among African Americans than among other populations. The Cohort Consortium also is investigating the influence of waist circumference on mortality among African Americans. Dr. Julie Palmer of the Boston University School of Public Health in Massachusetts is leading an effort to increase the study populations by adding cohorts with substantial numbers of African Americans. Members of the Cohort Consortium also are exploring the relation of BMI to mortality among Asian Americans.

In addition to examining the mortality effects of BMI in various populations, the Cohort Consortium is seeking to disentangle the role of obesity-related factors, including waist circumference, height, and physical activity. Although we know that physical activity affects the risks of obesity and mortality, the interplay of obesity, activity, and mortality remains uncertain. Dr. I-Min Lee of the Harvard School of Public Health, **Steven C. Moore, Ph.D.** (NEB), Dr. Alpa V. Patel of the American Cancer Society, and colleagues have recently pooled data from six cohorts in the Cohort Consortium that assessed physical activity for a total of 654,827 individuals and 82,465 deaths. Within each BMI category, they saw clear benefits of activity, even at the modest levels recommended in current guidelines (see Figure 1). The investigators are now extending the analysis to include additional cohorts in order to study risks of specific cancers. ■

—Patricia Hartge, Sc.D., and Victoria A. McCallum, M.P.H.

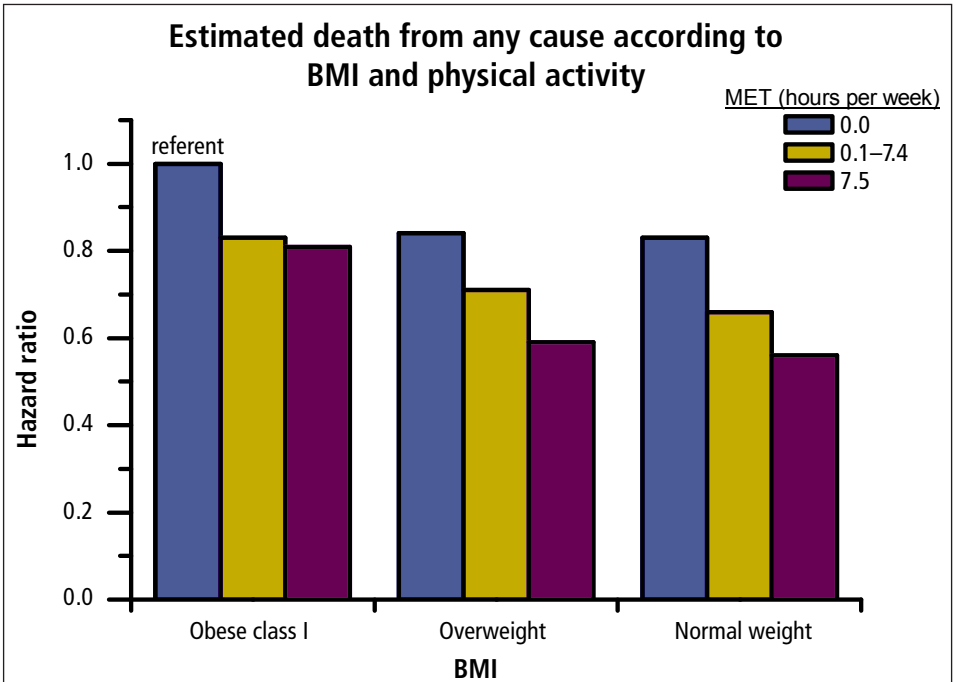


Figure 1. Estimated hazard ratios of death in relation to joint categories of body mass index (BMI) and physical activity. MET is the metabolic equivalent task. BMI is the weight in kilograms divided by the square of the height in meters. Obese class I is defined as a BMI of 30.0–34.9, overweight is a BMI of 25.0–29.9, and normal weight is a BMI of 18.5–24.9. (Moore SC, et al. 2011)

PREETHA RAJARAMAN EXPLORES ENVIRONMENTAL AND GENETIC RISK FACTORS

The only confirmed risk factors for brain tumors are exposure to ionizing radiation and certain rare genetic syndromes. With a strong background in environmental health and epidemiology, **Preetha Rajaraman, Ph.D.,** a tenure-track investigator in the Radiation Epidemiology Branch (REB), is exploring how environmental and genetic risk factors interact in the etiology of brain tumors.

Dr. Rajaraman is especially interested in biological pathways related to the development of radiogenic brain cancer. She has examined the risk of brain tumors with respect to candidate gene variants in selected mechanisms, including apoptosis, oxidative response, cell-cycle control, and DNA repair. Dr. Rajaraman currently is conducting a genome-wide association study (GWAS) to identify genetic markers of susceptibility to glioma, the most common type of brain tumor. She believes that some of the pathways that she and others have identified through GWAS are "quite exciting." She plans to follow up these associations by looking for potential interactions with environmental risk factors.

Dr. Rajaraman took a circuitous route to get to where she is today. After college, she worked at a wildlife reserve and at the Ministry of Health in Botswana. Her growing interest in health research led her to pursue training in environmental health at the University of Washington and to work at the Washington State Department of Labor and Industries, where she managed the Adult Blood Lead Epidemiology and Surveillance Program. When she joined the Ph.D. program in epidemiology at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, she pursued her interest in lead toxicity by examining data from an ongoing REB study of adult brain tumors, examining the unanswered question of whether lead exposure affects the risk of brain tumors. "The more I learned, the more I became intrigued by brain tumors themselves," Dr. Rajaraman said. "They can be such highly lethal tumors, and yet so little is known about them."

In 2004, Dr. Rajaraman completed her predoctoral fellowship in REB and became a postdoctoral fellow, where she enjoys the exciting intellectual environment offered at NIH. "Not only do you get to ask questions that may have a meaningful public health impact, but you're doing it in a great setting surrounded by many experts in different fields," she said.

Following her appointment in 2009 as a tenure-track investigator, Dr. Rajaraman joined the leadership team for the U.S. Radiologic Technologists Study, a cohort of approximately 150,000 technologists. In this study, Dr. Rajaraman is investigating the effects of low-dose fractionated exposure to ionizing radiation on the risk of breast and other cancers. The availability of blood samples within this cohort has allowed her to examine potential gene-radiation interactions in breast cancer. Dr. Rajaraman also is studying the risk of cancer and cardiovascular disease among technologists working with newer and higher dose radiological procedures, such as interventional fluoroscopy and nuclear medicine.

At the heart of many of Dr. Rajaraman's projects is the underlying theme of identifying susceptible populations. A particularly vulnerable population is young children. Thus, Dr. Rajaraman is examining the effects of radiation in

Preetha Rajaraman

population groups exposed early in life. Studies from the 1950s pointed to an increase in cancer risk for people who were exposed to diagnostic x-rays *in utero.* X-ray doses have decreased over time, and the risk of most cancers has followed suit. Nonetheless, using data from the United Kingdom Childhood Cancer Study, Dr. Rajaraman identified one type of cancer—acute myeloid leukemia—whose risk may still be increased by exposure to radiation.

To pursue her interest in the impact of radiation exposure in early life, Dr. Rajaraman is involved in the Childhood Cancer Survivor Study, in which a cohort of children exposed to cancer radiotherapy is being evaluated to identify potential gene-radiation interactions.

Dr. Rajaraman is developing a comprehensive strategy to identify both environmental and genetic risk factors for brain tumors. She believes that the discovery of heritable mechanisms may lead to potential drug targets that have preventive and/or therapeutic implications. Furthermore, the detection of lifestyle and other environmental factors in concert with genetic susceptibility may inform behavioral and other changes that reduce cancer risk. ■

—Erin M. Fults

MARK PURDUE SEEKS THE CAUSES OF CANCER

According to **Mark Purdue, Ph.D.,** a tenure-track investigator in the Occupational and Environmental Epidemiology Branch (OEEB), "My interest is in combining environmental epidemiology with molecular techniques to study the causes of cancer. DCEG and OEEB are on the cutting edge of such research." For Dr. Purdue, this is the ideal training and research environment.

After completing his doctorate in epidemiology at the University of Toronto in Ontario, Canada, with an investigation into how exposure to sunlight affects molecular subtypes of melanoma, Dr. Purdue came to OEEB as a postdoctoral fellow in 2004 and was promoted to tenure-track investigator in 2009. He is the co-principal investigator for DCEG research in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial and oversees use of its biospecimens for etiologic and early disease marker studies.

Dr. Purdue has been interested in investigating the causes of non-Hodgkin lymphoma (NHL), a cancer whose incidence has increased rapidly in recent decades. Patients with severe immune dysregulation, such as those who have HIV infection or are receiving strong immunosuppressive drugs for an organ transplant, have a high risk of NHL, and thus immunologic alterations may be an important mechanism driving increased risk. Because of this, "We were interested in conducting research within the general population to see if more subtle changes in immune regulation influence NHL risk," Dr. Purdue explained.

In a prospective study of 297 cases and 297 matched controls from the PLCO cohort, Dr. Purdue and his colleagues examined serum levels of soluble CD30, a suspected marker of B-lymphocyte activity. A strong dose-response relationship was seen between soluble CD30 serum levels and NHL risk; strikingly, the risk was increased significantly even 6 to 10 years after blood collection. As Dr. Purdue noted, "This finding is consistent with an etiologic association, not simply a disease-induced effect."

Dr. Purdue also is interested in investigating whether occupational and environmental exposures influence NHL risk. In particular, he is leading research into the effects of trichloroethylene (TCE), a solvent used to clean metal parts. TCE currently is classified by the International Agency for Research on Cancer (IARC) in group 2A (i.e., probably carcinogenic to humans). The evidence for this classification was based on studies in laboratory animals and was last reviewed by IARC in 1995.

In a case-control study of NHL within NCI's Surveillance, Epidemiology, and End Results (SEER) program, Dr. Purdue found that a high level of estimated occupational TCE exposure was significantly associated with increased risk. A particular strength of this study was the detailed methods used to estimate exposure. As Dr. Purdue explained, "It will be particularly important for IARC to have additional data from human studies for its next review of TCE, so our study should make an important contribution to this evaluation."

Dr. Purdue recently has expanded his work into studies of kidney cancer, another malignancy with increasing incidence. As with NHL, early evidence suggests an association between TCE and kidney cancer, and thus he is currently pursuing that lead. Recently, Dr. Purdue and colleagues published

Mark Purdue

the first genome-wide association study of renal cell carcinoma (RCC), the most common type of kidney cancer. In a study of 3,772 cases and 8,505 controls, Dr. Purdue joined forces with IARC investigators to identify two chromosomal regions associated with RCC susceptibility at a level of genome-wide significance. One locus, on chromosome 2p21, maps to the gene *EPAS1*, which has been found experimentally to influence RCC development. "The second locus is in 11q13.3, which has no characterized genes, so it is not clear what underlies the association," Dr. Purdue noted. "We are following up on these findings to seek a better understanding of the underlying mechanisms."

Dr. Purdue and his wife, Melissa, a sales representative for a company that markets laboratory instruments to clinical microbiology labs, have a daughter who is nearly 5 years old and an 8-month-old son. In his admittedly limited spare time, Dr. Purdue "shuttles the kids around," reads, and hikes. "It's a challenge juggling work and family, especially with small children," he said. "I find it rewarding and exhausting in equal measure." ■

—Terry Taylor, M.A.

NEW LEADERSHIP IN THE GENETIC EPIDEMIOLOGY BRANCH

In March, DCEG announced the appointments of **Neil E. Caporaso, M.D.,** as Chief of the Genetic Epidemiology Branch (GEB) and **Lynn R. Goldin, Ph.D.,** as Deputy Chief.

Dr. Caporaso, who received his M.D. from the University of Medicine and Dentistry of New Jersey, is board certified in both internal medicine and medical oncology. He joined NCI in 1983 as an oncology fellow in the Medicine Branch and later served as a research fellow and biotechnology fellow in the Environmental Epidemiology Branch. Since 1991, he has been a tenured principal investigator in GEB, where his research has focused on smoking behaviors and the molecular epidemiology of lung cancer as well as the etiology of leukemia and related hematologic and lymphoproliferative conditions. Dr. Caporaso has published extensively in high-impact journals and has served as an inspiring mentor to numerous other scientists. His scientific vision and leadership qualities should help to ensure GEB's future success.

Neil Caporaso and Lynn Goldin.

Dr. Goldin, who received her Ph.D. in genetics from the University of North Carolina at Chapel Hill, worked in the Clinical Neurogenetics Branch of the National Institute of Mental Health before joining GEB in 1998 as a tenured principal investigator. Her major research interests are in developing and evaluating statistical methods and study designs for detecting susceptibility genes in complex diseases, quantifying familial aggregation of disease, and applying the methods of genetic epidemiology to studies of familial cancer syndromes. She will provide scientific leadership and managerial support to GEB. ■

KATHERINE MCGLYNN APPOINTED DEPUTY BRANCH CHIEF

Katherine McGlynn

In February, **Katherine A. McGlynn, Ph.D., M.P.H.**, was named Deputy Chief of the Hormonal and Reproductive Epidemiology Branch (HREB). Dr. McGlynn received an M.P.H. in population studies from Tulane University in New Orleans, Louisiana, and a Ph.D. in epidemiology from the University of Pennsylvania in Philadelphia. She served as a faculty member at Fox Chase Cancer Center in Philadelphia before joining DCEG, where she was tenured as a senior investigator in 2008. Dr. McGlynn's research has focused on the molecular epidemiology of testicular and liver cancer. In 2010, in recognition of her scientific accomplishments, she was elected as a member in the American Epidemiological Society.

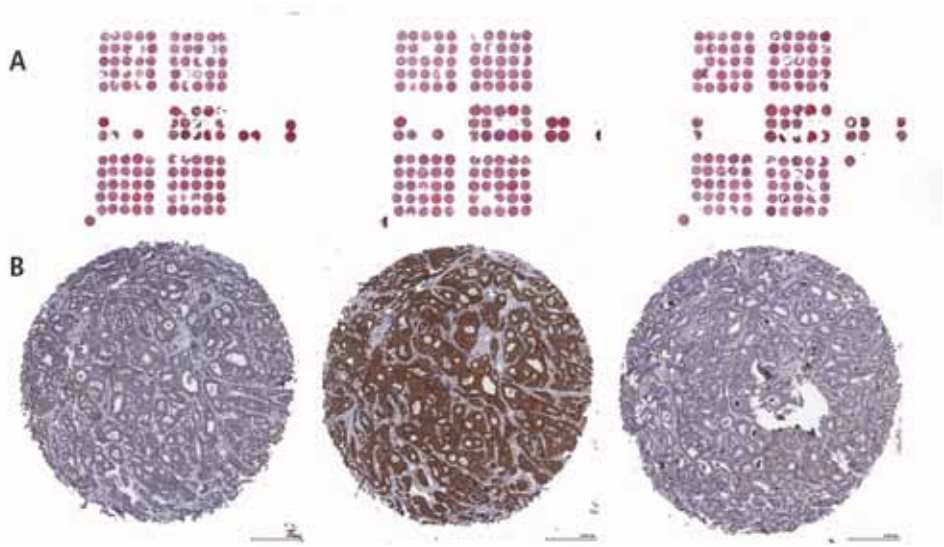
In addition to her scientific expertise, Dr. McGlynn brings considerable management and strategic planning skills to HREB, having served as Chair of the DCEG Committee of Scientists for the past four years. As Deputy Chief, she will assume responsibility for several Branch activities, including oversight of HREB's Distinguished Lecturer program, scientific presentations at Branch and Division meetings, and assurance of compliance with requirements for the proper conduct of studies. She also will play a key role in recruitment activities and the mentoring and training of junior investigators.

ENRICHING EPIDEMIOLOGY THROUGH MOLECULAR PATHOLOGY

Large-scale analyses of tumor tissue samples can contribute greatly both to molecular epidemiologic investigations aimed at defining the causes of cancer and the mechanisms that mediate them as well as to translational studies that seek to apply this knowledge to improve public health or clinical management.

The Applied Molecular Pathology Laboratory (AMPL), an interdisciplinary effort initiated in 2009 and funded jointly by DCEG and the Center for Cancer Research (CCR), is a high-throughput lab that designs and constructs tissue microarrays (TMAs) and develops and implements other promising tissue-based molecular assays in a validated, standardized fashion. It was developed to apply standardized testing to thousands of tissue specimens concurrently in support of large intramural studies in DCEG and CCR.

Studying tissue samples collected from tumors presents some special challenges. "Tumors are not homogeneous all the way through, so it is important to extract samples from the location in the tumor that will render the most information," explained **Mark E. Sherman, M.D.,** of the Hormonal and Reproductive Epidemiology Branch, who is the DCEG point person for the AMPL. "Studying these samples requires knowledge of both histopathology [i.e., the microscopic appearance of cells and tissues] and applied molecular pathology [i.e., applying molecular biology techniques to diagnostic, therapeutic, or etiologic research]," he said. "Pathologists first seek to define what normal cells look like and how they function in order to be able to identify precancerous and cancerous cells and how they malfunction."



A: Tissue microarrays containing hundreds of tissue cores can enable the rapid examination of thousands of subjects' specimens in large-scale studies. B: Individual tissue cores are stained with various immunohistochemical stains to aid in analysis.

One technique employed in the AMPL that is aptly suited for large studies is the construction of TMAs, which consist of cores of tissue extracted from tumor samples that are then inserted through a precise matrix into a new tissue block. Each block contains cores from hundreds of tumors. Sections that are cut from TMA blocks can be affixed to slides and treated with immunohistochemical stains designed to point out specific markers. Stained slides are scanned to generate digital images for review and analysis. One of the AMPL's first accomplishments in its pilot phase was the creation of TMAs from the Polish Breast Cancer Study. These TMA blocks represent a total of 7,800 cores and comprise a resource that can be used to perform batched analyses of hundreds of tissue markers.

Tissue specimens can be quite variable with respect to preparation and storage, especially if samples were collected years ago. Despite challenges, many of these archived specimens are valuable because they are linked to clinical outcomes.

"Over the past 10 years, we have learned much from working with archival samples—we have developed optimal techniques for building microarrays, producing slides, and performing assays on materials, and we have more effective tools to help us moving forward," commented Stephen M. Hewitt, M.D., Ph.D., from the CCR Laboratory of Pathology, who runs the lab on a daily basis. "The archival samples also provide a large resource for reference today," he said. "When we work with clinical samples and identify a biomarker that may predict an outcome, we can test it in a large archival set to validate it."

As research projects move forward, the potential for continued progress will depend on how well current initiatives succeed in standardizing the collection and storage of tissue as well as on technologic improvements in tissue handling and analysis. The early inclusion of pathologists in the design and planning of new epidemiological and translational studies will help to optimize the use of these new techniques. ■

—Wendy Schneider-Levinson

25TH ANNIVERSARY OF CHERNOBYL ACCIDENT

On April 26, 1986, an accident at the Chernobyl nuclear power plant in what is now Ukraine caused an explosion and the subsequent release of radioactive materials. More than 28 emergency workers at the plant died within the first four months as a result of exposure to extremely high levels of radiation. Across the region, more than 6 million people in Belarus, Russia, and Ukraine were exposed to varying levels of radiation from radioactive fallout, principally radioactive iodine (I-131) and cesium-137. Plant staff and emergency workers, clean-up workers (also known as liquidators), and children living in the contaminated areas experienced the largest share of adverse health effects from the accident.

Dr. Gilbert W. Beebe (1912–2003), a health statistician in the epidemiology program from which DCEG was created, played a leading role in launching multidisciplinary, collaborative projects to study the health consequences of the accident. Dr. Beebe and fellow NCI staff, along with many international radiation experts as well as investigators from Belarus and Ukraine, designed epidemiologic studies on the exposed populations. These studies, carried out with research partners at Columbia University in New York City, became part of DCEG's Radiation Epidemiology Branch (REB) portfolio in 1995 and included:

- Two cohort studies of the long-term risk of thyroid cancer and other diseases among individuals in Ukraine and Belarus who were children or adolescents at the time of the accident and received relatively high doses of radioiodines. Later, individuals who were exposed *in utero* were added to the studies.
- A case-control study of leukemia among a cohort of clean-up workers in Ukraine who were exposed mostly to external gamma radiation over a protracted period of time.

For these studies, REB dosimetrists worked closely with Belarusian and Ukrainian scientists, as well as epidemiologists, to reconstruct individual radiation dose estimates, which formed the basis for quantifying the radiation-related cancer risks. In addition, two external advisory groups—the Leukemia Advisory Group and the Thyroid Advisory Group—were formed to provide ongoing peer review and scientific oversight for the studies.

"Even 20 years after the accident, we see a persistently increased risk of thyroid cancer attributable to radioactive iodine."

What Have We Learned from the Chernobyl Accident?

Dozens of papers have been published from these studies, describing their methodology and findings. "From the study of accidents such as Chernobyl, we can develop better understanding of the dose-dependent risk of adverse health effects, including both internal exposure to radioactive iodine and chronic external radiation exposure," said **Kiyohiko Mabuchi, M.D., Dr.P.H.,** Deputy Chief of REB and head of the Chernobyl Research Unit. "Even 20 years after the accident, we see a persistently increased risk of thyroid cancer attributable to radioactive iodine," said **Maureen C. Hatch, Ph.D.** (REB), former head of the Chernobyl Research Unit.

Investigators used sophisticated models and measurements of thyroid radiation activity to develop reliable dose estimates and conducted standardized screening to identify cancer cases, which enabled them to estimate the risk from radiation exposure in the cohort of children and adolescents. The risk of thyroid cancer increased with radiation dose from I-131 throughout the study period of 1998 to 2007. The primary source of radioactive iodine among the children was from drinking milk produced by cows that had eaten contaminated grass.

Among clean-up workers in Ukraine, who were exposed to protracted low-dose radiation, the risk of leukemia also increased with radiation dose, and the magnitude of the risk was comparable to that of atomic bomb survivors, who experienced acute radiation exposure. Without a cancer registry in Ukraine at the time of the study's initiation, investigators identified leukemia cases by visiting a large number of medical institutions in various localities, and they confirmed the diagnoses through a review by a panel of international hematology experts. Doses were reconstructed based on data gathered through extensive interviews about work histories, because exposures differed by the type, duration, location, and timing of jobs performed after the accident.

Findings from these studies are contributing greatly to the ongoing development of standards for radiological protection and countermeasures needed in the event of a nuclear accident.

For detailed information on the Chernobyl studies, go to http://chernobyl.cancer.gov. ■

—Jennifer Loukissas, M.P.P., and Wendy Schneider-Levinson

2011 RADIATION EPIDEMIOLOGY AND DOSIMETRY COURSE

In May, the Radiation Epidemiology Branch (REB) welcomed a large and diverse audience to its course Radiation Epidemiology and Dosimetry, which is offered by the Branch every three to four years to promote education in radiation sciences, research training, and mentoring. This year's course drew approximately 180 participants, a 40 percent increase in attendance from 2007, when the course was last given.

The three-day course included in-depth presentations on concepts in radiation epidemiology and dosimetry as well as updates on the recent major studies that have contributed new scientific insights. Cancer risks associated with environmental radiation were emphasized, including new data from studies of the atomic bomb survivors and Chernobyl exposures, as well as strategies for radiation risk assessment and modeling. Exposures from nuclear accidents were discussed, with special attention paid to the recent disaster that followed the earthquake in Japan. Advances in physical and biologic dosimety, along with mitigation procedures, were covered.

In addition, epidemiologic studies of the cancer risks associated with diagnostic and therapeutic radiation were presented. Attention was given to the susceptibility of children to risks associated with diagnostic radiation exposures. There also was a session on the potential health effects of exposure to electromagnetic fields, cell phones, and ultraviolet radiation.

Radiation Epidemiology Course Coordinating Committee: (front) Rochelle Curtis, Martha Linet, and D. Michal Freedman; (back) Alina Brenner, Alice Sigurdson, Abigail Ukwuani, and Vladimir Drozdovitch. (Not shown: Jenna Nober.)

According to **Alice J. Sigurdson, Ph.D.** (REB), course director, REB offered two new components this year based on feedback from past attendees. The first was a half-day session on how to use EPICURE software programs for statistical modeling of radiation risk, and the second was a one-day minicourse on the basic concepts of radiation epidemiology and dosimetry.

Course instructors included radiation epidemiologists, dosimetrists, statisticians, and radiobiologists from DCEG and elsewhere. In addition to Dr. Sigurdson, the organizing committee (all from REB) included **Martha S. Linet, M.D., M.P.H.,** Chief of REB; **Alina V. Brenner, M.D., Ph.D.; Rochelle E. Curtis, M.A.; Vladimir Drozdovitch, Ph.D.; D. Michal Freedman, Ph.D., M.P.H.; Jenna Nober;** and **Abigail Ukwuani, M.P.A.** ■

—Alice J. Sigurdson, Ph.D., and Abigail Ukwuani, M.P.A.

DCEG RESPONDS TO JAPAN'S NUCLEAR CRISIS

For two weeks during March, **Steven L. Simon, Ph.D.,** Radiation Epidemiology Branch, was deployed to Tokyo, Japan, with a U.S. Department of Health and Human Services medical and health team sent by the Assistant Secretary for Preparedness and Response, Dr. Nicole Lurie. The team's primary mission was to provide advice to personnel at the U.S. embassy and consulates in Japan on health issues related to radiation exposure following the earthquake, tsunami, and damage to a nuclear power plant at Fukushima Daiichi. Approximately 150,000 American citizens are living in Japan, and Dr. Simon and his colleagues addressed a range of questions to help these individuals make informed health and safety decisions. These questions included concerns about possible contamination of food and water, the potential use of potassium iodide to prevent exposure of the thyroid to radiation, the evaluation of radiation levels in Tokyo, and the conditions for relocation and reentry into the area after voluntary evacuation. In addition, the leadership at the embassy arranged for the team to deliver multiple public briefings on radiation health issues.

The team members included Captain Thomas Bowman of the Centers for Disease Control and Prevention (CDC); C. Norman Coleman, M.D., from the NCI Division of Cancer Treatment and Diagnosis; Captain Michele Hancock of the U.S. Navy; Dr. Michael Noska of the U.S. Food and Drug Administration; and Ms. Jana Telfer (CDC). Following his return to NIH, Dr. Simon gave a seminar on his experiences in Japan. He continues to provide advice and to monitor radiation levels collected from a device installed on the embassy roof by scientists from the U.S. Department of Energy.

THIRD ANNUAL DCEG FELLOWS' TRAINING SYMPOSIUM

March 2011 marked the third annual DCEG Fellows' Training Symposium, titled Shaping Future Research: Provocative Questions in Cancer Epidemiology and Genetics. The event was sponsored by DCEG's Office of Education (OE) and organized by a DCEG fellows committee, including cochairs **Todd M. Gibson, Ph.D.,** Radiation Epidemiology Branch (REB), and **Shih-Wen (Wenny) Lin, Ph.D., M.P.H.,** Nutritional Epidemiology Branch (NEB), as well as **Paula Hyland, Ph.D., M.P.H.,** Genetic Epidemiology Branch, **Gabriel Lai, Ph.D.** (NEB), **Gila Neta, Ph.D., M.P.P.** (REB), **Christina Persson, Ph.D.,** Hormonal and Reproductive Epidemiology Branch, and **Meredith Shiels, Ph.D., M.H.S.,** Infections and Immunoepidemiology Branch, with support from **Jackie Lavigne, Ph.D., M.P.H.,** Chief of OE, **Kristin Kiser, M.H.A., M.S.** (OE), and **Tess Lee** (OE). The aim of the symposium was to follow up on the "Provocative Questions" initiative of NCI Director Harold Varmus, M.D. More than 70 predoctoral and postdoctoral fellows, representing all of the DCEG units, participated in the event.

Dr. Jonathan M. Samet, professor and Flora L. Thornton Chair of the Department of Preventive Medicine at the Keck School of Medicine, University of Southern California, began the symposium with the lecture "Cancer: A neglected global health problem." Dr. Samet spoke on opportunities for cancer prevention, early detection, and treatment in the context of global health and provided examples of provocative questions, ranging from the global and national (i.e., upstream) levels to the family and individual (i.e., downstream) levels.

In "Epidemiologic challenges: Confounding our future," Dr. Margaret Spitz of the MD Anderson Cancer Center in Houston, Texas, and special advisor to DCEG, discussed provocative questions in molecular epidemiology, including the hereditary components of cancer and the biological basis of cancer susceptibility, the mechanisms that link energy balance and obesity to cancer, and the relationships between the human microbiome and cancer.

Margaret Spitz, John Groopman, and Jonathan Samet.

Dr. John Groopman, the Anna M. Baetjer Professor and chair of the Department of Environmental Health Sciences at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, discussed "Translating molecular sciences to public health prevention strategies." He encouraged fellows to take a long-term approach to thinking about cancer prevention and described examples of recent advances in cancer genomics and epigenomics, the exposome, and population studies that can inform the discovery and validation of biomarkers. The afternoon began with a spirited panel discussion in which all three speakers responded to a variety of questions that dealt with scientific opportunities and advice.

Two poster sessions featured the research projects of more than 40 fellows, while further discussions were held during lunch to enable fellows to generate and exchange their ideas for provocative questions in cancer epidemiology and genetics. In addition, two fellows gave oral presentations selected by the planning committee for scientific merit, originality, and innovation. Dr. Lai spoke on "The association between diabetes and cancer incidence and mortality in the NIH-AARP Study," while **Stephanie Lamart, Ph.D.** (REB), spoke on "Improvements in estimating radiation doses to adult patients treated with I-131." **Joseph F. Fraumeni, Jr., M.D.,** Division Director, concluded the symposium with a presentation titled "Scanning the horizon," in which he described the opportunities and challenges that lie ahead for the DCEG scientific staff.

All of the participants agreed that the day was a great experience during which they learned about the range of scientific projects carried out by fellows across the Division and heard about the tremendous variety of future opportunities in the field from leading scientists. ■

—Todd M. Gibson, Ph.D.,
and Shih-Wen (Wenny) Lin, Ph.D., M.P.H.

ELAINE RON MEMORIAL SYMPOSIUM

Elaine Ron, Ph.D., former Chief and senior investigator, Radiation Epidemiology Branch (REB), was honored posthumously at a symposium titled "Research Strategies in Radiation and Cancer" on March 9. An international leader in the field of radiation epidemiology, Dr. Ron died of cancer on November 20, 2010.

Joseph F. Fraumeni, Jr., M.D., DCEG Director, provided the opening remarks, noting that "Elaine was an enormously gifted epidemiologist whose groundbreaking research has contributed so much to a better understanding of the risks of cancer associated with a wide variety of exposures to ionizing radiation." **Martha S. Linet, M.D., M.P.H.,** Chief of REB, also offered remarks on the life and legacy of Dr. Ron, highlighting the progression of her research over the years.

A group of Dr. Ron's collaborators and peers reflected on her major contributions to radiation epidemiology studies in a session titled "Successful research strategies in radiation." Moderated by **Kiyohiko Mabuchi, M.D., Dr.P.H.,** Deputy Chief of REB, the panel discussed four studies in particular: (1) the Life Span Study, which followed survivors of the Hiroshima and Nagasaki bombings; (2) the tracking of the aftermath of the Chernobyl nuclear disaster, which involved extensive collaborations with Ukrainian and Belarusian scientists; (3) a landmark pooled analysis examining radiation exposure and the risk of thyroid cancer; and (4) an ongoing investigation evaluating cancer risk following childhood exposure to computed tomography scans. Members of the panel included Dr. David Brenner, Director of the Center for Radiological Research at Columbia University in New York City; Dr. Silvia Franceschi from the International Agency for Research on Cancer (IARC) in Lyon, France; Dr. Shirley Fry, an epidemiology consultant; Dr. Charles Land, formerly of REB; Dr. Dale Preston, a consultant with Hirosoft International Corporation, Inc.; and Dr. Arthur Schneider, Professor Emeritus of Medicine in the Department of Medicine at the University of Illinois at Chicago.

Successful Research Strategies in Radiation panel members: Arthur Schneider, Shirley Fry, Charles Land, Silvia Franceschi, Dale Preston, David Brenner, and Kiyohiko Mabuchi (moderator).

At a second panel, titled "Mentoring and training for successful strategies in radiation research," members spoke about Dr. Ron as a role model and the dedicated mentoring she provided throughout her career. **Shelia Hoar Zahm, Sc.D.,** Deputy Director of DCEG, moderated the panel of former and current DCEG fellows, including Dr. Gabriel Chodick from the Tel Aviv University's School of Public Health in Israel; **Evgenia Ostroumova, M.D., Ph.D.** (REB); Dr. Cecile Ronckers of the Dutch Childhood Oncology Group located in The Hague, The Netherlands; **Sara Schonfeld, Ph.D.** (REB); and Dr. Lene H.S. Veiga from the Brazilian Nuclear Energy Commission in Rio de Janeiro. All of the panel members spoke about Dr. Ron's extraordinary capacity to reach out and influence a new generation of radiation epidemiologists on a global scale.

A panel of REB investigators then presented a session titled "Evolving research strategies in radiation" that highlighted new directions that are likely to accelerate progress in the field of radiation epidemiology. Speakers were **Amy Berrington de González, D.Phil.; Alina V. Brenner, M.D., Ph.D.; Choonsik Lee, Ph.D.; Lindsay M. Morton, Ph.D.;** and **Preetha Rajaraman, Ph.D.**

Finally, Dr. Christopher Wild, director of IARC—where Dr. Ron served on the Scientific Council—discussed "Two-way translational research: From basic science to both the clinic and the population," with an emphasis on the study of radiation-exposed populations around the world. **Margaret A. Tucker, M.D.,** Director of the DCEG Human Genetics Program, closed the symposium by offering tributes to Dr. Ron's life and career. ■

—Victoria A. McCallum, M.P.H.

DCEG RESEARCH HIGHLIGHTED AT ANNUAL AACR MEETING

In April, DCEG members participated in the 102nd Annual Meeting of the American Association for Cancer Research (AACR) in Orlando, Florida. This five-day event provided a forum to highlight the latest scientific advances in basic, clinical, and epidemiologic cancer research. The theme of this year's meeting was Innovation and Collaboration: The Path to Progress.

Stephen J. Chanock, M.D., Chief of the Laboratory of Translational Genomics (LTG) and Director of the Core Genotyping Facility (CGF), gave a plenary presentation titled "The heritable component of cancer: Insights from genome-wide association studies and beyond." **Maria Teresa Landi, M.D., Ph.D.,** Genetic Epidemiology Branch, cochaired the symposium "Host and lifestyle factors in cancer risk." During this session, **Katherine A. McGlynn, Ph.D., M.P.H.,** Deputy Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), presented a talk titled "Metabolic syndrome increases the risk of primary liver cancer in the United States," and **Gabriel Lai, Ph.D.,** Nutritional Epidemiology Branch (NEB), spoke on "The association between diabetes and cancer incidence and mortality in the NIH-AARP Study." Both of these presentations were highlighted by AACR for press attention.

Other symposium presenters included **Alison Mondul, Ph.D.** (NEB), who discussed "Genetic determinants of serum retinol: A genome-wide association study." In addition, **Nilanjan Chatterjee, Ph.D.,** Chief of the Biostatistics Branch, chaired the session "Statistical challenges of analyses of genome-wide data" and presented "Statistical issues in post-GWAS analyses." The session also included **Kevin B. Jacobs, M.S.** (CGF), who spoke on "Analysis of studies of germline variation using next-generation sequencing and genotyping."

Two DCEG staff gave presentations on career development topics: **Jackie Lavigne, Ph.D., M.P.H.,** Chief of the Office of Education, spoke on "Fellowship opportunities in cancer epidemiology and genetics," and **Jill Koshiol, Ph.D.,** Infections and Immunoepidemiology Branch, presented "Choosing the right postdoctoral fellowship/clinical fellowship for research careers in academia, industry, and government." In addition, **Louise A. Brinton, Ph.D.,** Chief of HREB, chaired a roundtable session on "Women in cancer research career mentoring."

DCEG scientists presented approximately 40 posters. **Lisa Mirabello, Ph.D.,** Clinical Genetics Branch, was selected as a finalist for an AACR Scholar-in-Training Award for her poster "Methylation of the HPV 16 L1 gene is associated with disease progression in a prospective population-based cohort." Mia M. Gaudet, Ph.D., a former fellow of HREB, and her DCEG colleagues received special recognition for their poster "Serum metabolic profiles and endometrial cancer," which was based on the Polish Women's Health Study. Other abstracts selected for media attention included those of **Kelly L. Bolton, M.Phil.** (LTG), on "Genetic heterogeneity of ovarian cancer survival effects of BRCA1/2 germline mutations" and of **Christina Persson, Ph.D.** (HREB), on "Risk of esophageal and stomach cancer in people with AIDS."

DCEG investigators also led or participated in a variety of collaborative research groups held in conjunction with the AACR meeting. Several groups met to review progress and plan projects, including the North American Li-Fraumeni Syndrome Research Consortium, the Epidemiology of Endometrial Cancer Consortium, PRACTICAL (*Pr*ostate cancer *a*ssociation group *t*o *i*nvestigate *c*ancer *a*ssociated a*l*terations in the genome), and the Asia Cohort Consortium. ■

—Saloni Nayar, M.P.H.

FALL 2010 INTRAMURAL RESEARCH AWARDS

DCEG Intramural Research Awards (IRAs) are competitive funding opportunities designed to foster creative, high-impact research by fellows and tenure-track investigators. Proposals are evaluated by members of the Board of Scientific Counselors on their potential for significant scientific or public health impact, innovation, interdisciplinary nature, ability to achieve the objectives within the proposed time frames and resources, and programmatic relevance to DCEG's mission. Funding may be up to $50,000 per proposal. From the many excellent proposals submitted for IRAs during the fall 2010 competition cycle, the following lead investigators and their proposals were selected:

Aimee Kreimer, Ph.D., Infections and Immunoepidemiology Branch: *Prospective evaluation of human papillomavirus infection prior to the diagnosis of head and neck cancer*

Wei Tang, Ph.D., Laboratory of Translational Genomics: *Functional annotation of non-coding region in* JAZF1 *as a regulatory element*

David Wheeler, Ph.D., M.P.H., Occupational and Environmental Epidemiology Branch: *Spatial-temporal cluster analysis of non-Hodgkin lymphoma in the NCI-SEER Study*

DCEG SCIENTISTS PARTICIPATE IN ISBER ANNUAL MEETING

On May 15–18, the International Society for Biological and Environmental Repositories (ISBER) held its 12th annual meeting in Arlington, Virginia. Titled Impact and Public Benefits of Biorepositories, the meeting featured plenary sessions, educational workshops, corporate workshops, contributed papers, poster sessions, vendor exhibits, and working group discussions.

ISBER is the leading international forum for addressing the technical, legal, ethical, and managerial issues relevant to repositories of biologic and environmental specimens. DCEG is a founding member of ISBER, and several DCEG staff members play key roles in the Society and spoke at the annual meeting.

Marianne Henderson receives the gavel from ISBER Past President Scott Jewell.

The leadership gavel was presented to **Marianne K. Henderson, M.S.,** Chief, Office of Division Operations and Analysis, who was inducted as the President of ISBER (2011–2012) at the meeting. She is serving the second year of her three-year term in the leadership of the ISBER Council and was a member of the planning committee for this year's meeting. **Karen E. Pitt, Ph.D.,** Office of the Director, serves on ISBER's Education and Training Committee and co-leads the effort to establish a certification program for repository technicians. At the meeting, Dr. Pitt received a Special Service Award for being part of the editorial team of the third edition of the *ISBER Best Practices*.

Nathaniel Rothman, M.D., M.P.H., M.H.S., a senior investigator in the Occupational and Environmental Epidemiology Branch, gave the meeting's keynote presentation, titled "The search for early biologic effect biomarkers and future risk of cancer: Molecular epidemiology and its impact on public health."

Allan Hildesheim, Ph.D., Chief of the Infections and Immunoepidemiology Branch, gave a talk on the "Challenges and rewards of molecular epidemiology studies in international settings." In addition, Mr. Tim Sheehy of SAIC led a poster presentation titled "High-throughput DNA and RNA extraction and processing by the DCEG DNA extraction and sample handling laboratory can yield increases in efficiency and savings." The poster was authored by Ms. Henderson, Ms. Sally Larson (SAIC), Dr. Pitt, and Mr. Sheehy.

Next year's ISBER annual meeting will be held in Vancouver, Canada. ■

—Marianne K. Henderson, M.S.

KATHERINE MCGLYNN PRESENTS NIH DIRECTOR'S SEMINAR

On March 18, **Katherine A. McGlynn, Ph.D., M.P.H.,** Deputy Chief of the Hormonal and Reproductive Epidemiology Branch, presented a lecture titled "Epidemiology of testicular germ cell tumors: Hormonal aspects" for the prestigious NIH Director's Seminar Series. Michael Gottesman, M.D., NIH Deputy Director for Intramural Research, introduced Dr. McGlynn and remarked on her considerable expertise and leadership in the field. Much of Dr. McGlynn's research has focused on understanding the origins of testicular germ cell tumors, the most common cancer among young men in the United States. Her presentation emphasized studies into the effects of early life exposures and hormonal risk factors, including the potential role of endocrine-disrupting chemicals. To view Dr. McGlynn's lecture, go to http://go.usa.gov/2us (case sensitive).

Katherine McGlynn and Michael Gottesman.

BROCHURE TO RAISE AWARENESS ABOUT SKIN CANCER AMONG MINORITIES

DCEG recently published a new brochure, *Anyone Can Get Skin Cancer,* designed to raise awareness of the risk for skin cancer among people with darker skin. The first NCI publication of its kind, it is a unique educational resource specific to darker skinned populations. The brochure, which is intended for African Americans, Asian Americans, Native Americans, and Hispanics/Latinos, was developed to help reduce morbidity and mortality from skin cancer among these groups.

Dr. Porcia Bradford, a former fellow in the Genetic Epidemiology Branch (GEB) whose research at DCEG focused on melanoma and other skin cancers, created a prototype of this brochure when she observed a lack of educational materials targeted to minority

Porcia Bradford

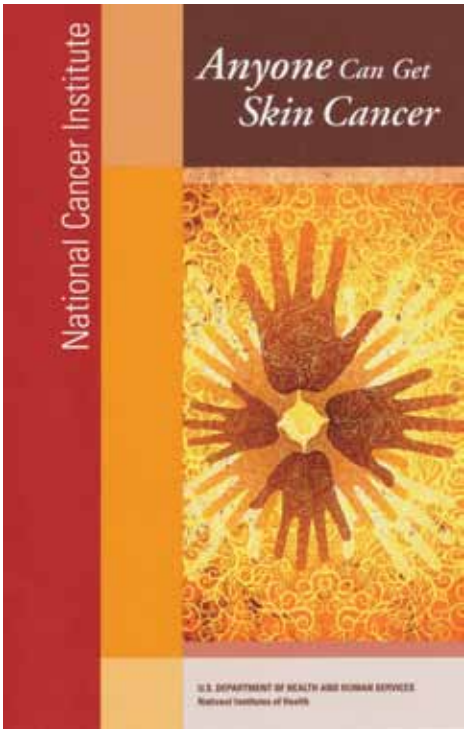
populations. Dr. Bradford is currently a dermatology resident at Duke University Health System in Durham, North Carolina.

Although the incidence of skin cancer among U.S. minorities is lower than that of the non-Hispanic white population, it is often detected at more advanced stages and is more likely to be fatal. In addition, the early signs and anatomic sites of skin cancer may appear differently in people with darker skin.

Anyone Can Get Skin Cancer aims to dispel the belief that only people with light skin are at risk for skin cancer. The publication discusses risk factors for skin cancer and encourages prevention and early detection behaviors. Highlights of the brochure are its presentations of real-life images of skin cancer among people with darker skin and a discussion of the manifestations of skin cancer unique to these populations.

The brochure represents a hallmark communications effort that is grounded in evidence-based strategies for educational materials. **Jennifer Loukissas, M.P.P.,** and **Saloni Nayar, M.P.H.,** both of the DCEG Office of Communications and Special Initiatives, along with a team of communications experts from NCI's Office of Communications and Education, managed the development and production of the brochure. **Mary C. Fraser, R.N., M.A.** (GEB), and **Margaret A. Tucker, M.D.,** Director of the Human Genetics Program, helped simplify the scientific content in Dr. Bradford's original prototype and finalize the brochure in plain language. Multiple focus groups that were conducted with diverse audiences provided feedback on the brochure's design and confirmed that the material was both easy to read and culturally appropriate.

"*Anyone Can Get Skin Cancer* meets a real need for these communities," Dr. Tucker said. "We hope it will help improve skin cancer prevention and early detection efforts among physicians and the public."



The *Anyone Can Get Skin Cancer* brochure is available in English and Spanish.

According to **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, "Great credit goes to Dr. Bradford for identifying this gap and translating her epidemiologic research into prevention strategies that will reduce cancer health disparities."

Anyone Can Get Skin Cancer is available in both English and Spanish editions and will be distributed to the public through health professional and advocacy groups. Various NCI and NIH channels, including a partnership with the National Center on Minority Health and Health Disparities, are helping to disseminate the brochure. To view the content online or to order a free copy, visit www.cancer.gov/anyone-can-get-skin-cancer. ■

—Saloni Nayar, M.P.H.

SCIENTIFIC HIGHLIGHTS

AIDS-RELATED CANCER

Cancer Among the HIV-infected

Purpose: As a result of effective antiretroviral therapy, more HIV-infected people are surviving long enough to be at risk for non–AIDS-defining cancers that typically occur at older ages. This study estimated the annual number of cancers in the HIV-infected population, both with and without AIDS, in the United States. **Methods:** The authors obtained estimated counts of individual AIDS-defining and non–AIDS-defining cancers in the AIDS and HIV-infected populations through the HIV/AIDS Cancer Match Study, which links data from the U.S. population-based HIV and cancer registries. **Results and conclusions:** In the AIDS population, the number of AIDS-defining cancers declined sharply between 1991 and 1997, with more gradual decreases in subsequent years (see Figure 1 on page 18). Notwithstanding these decreases, KS and NHL remain the most common malignancies in the U.S. AIDS population. The number of non–AIDS-defining cancers increased steadily from 1991 to 2005 and, since 2003, has exceeded the annual number of AIDS-defining cancers. The steep increase in non–AIDS-defining cancers among the HIV-infected population has largely been driven by the growth and aging of that population. **(Shiels MS, Pfeiffer RM, Gail MH, et al. Cancer burden in the HIV-infected population in the United States. *J Natl Cancer Inst* 2011;103:753–762)**

Impact of HIV on Cancer in the United States

Purpose: To quantify the impact of HIV on the total number of U.S. cases of certain AIDS-defining cancers (KS, diffuse large B-cell lymphoma [DLBCL], Burkitt lymphoma [BL], central nervous system [CNS] lymphoma, and cervical cancer), the authors determined the proportions of these cancers that occurred among people with AIDS from 1980 to 2007 as compared to the total number of cases that occurred in the United States. **Methods:** The authors obtained estimated counts from the HIV/AIDS Cancer Match Study (1980–2007) and derived cancer rates for people with and without AIDS. To estimate national counts, they applied the rates to national AIDS surveillance and U.S. census data. **Results and conclusions:** In the United States, HIV contributed substantially to the total numbers of the cancers in question; 82% of KS cases, 6% of DLBCL, 20% of BL, 27% of CNS lymphomas, and 0.4% of cervical cancer cases occurred among people with AIDS from 1980 to 2007. The proportion of these cancers with AIDS was highest in the mid-1990s and then declined, likely due to the introduction of highly active antiretroviral therapy in 1996. A higher proportion of cases with AIDS occurred among people less than 60 years old than among people older than 60. **(Shiels MS, Pfeiffer RM, Hall HI, et al. Proportions of Kaposi sarcoma, selected non-Hodgkin lymphomas, and cervical cancer in the United States occurring in persons with AIDS, 1980-2007. *JAMA* 2011;305:1450–1459)**

BLADDER CANCER

GSTM1 and *NAT2* Genes and Smoking

Purpose: To investigate associations of the *GSTM1*, *GSTT1*, and *NAT2* genotypes, as well as smoking, with bladder cancer risk. **Methods:** In the New England Bladder Cancer Study, the authors collected mouthwash samples for DNA extraction from 1,088 cases and 1,282 controls for genotype analysis of *GSTM1, GSTT1,* and *NAT2* polymorphisms. They also updated a meta-analysis of *NAT2* variants, smoking, and bladder cancer risk, based on 7,961 cases and 13,819 controls. **Results and conclusions:** ORs for bladder cancer among subjects with one or two inactive *GSTM1* alleles were 1.26 and 1.54, respectively, compared to those with two active copies. Inactive *GSTT1* alleles were not associated with risk, nor was *NAT2* slow acetylation status among never, former, or current smokers. However, among slow acetylators who ever smoked at least 40 cigarettes/day, risk was elevated among ever (OR = 1.82) and current heavy smokers (OR = 3.16). The effect of the *GSTM1*-null genotype was not greater among smokers, regardless of intensity. Meta-analysis of the *NAT2* associations with bladder cancer showed a highly significant relationship. **(Moore LE, Baris DR, Figueroa JD, et al. *GSTM1* null and *NAT2* slow acetylation genotypes, smoking intensity and bladder cancer risk: Results from the New England Bladder Cancer Study and *NAT2* meta-analysis. *Carcinogenesis* 2011;32:182–189)**

BREAST CANCER

Breast Cancer Risk in Asian and Pacific Islander American Women

Purpose: To develop a model for projecting absolute invasive breast

GLOSSARY

BMI	body mass index
CI	confidence interval
HR	hazard ratio
KS	Kaposi sarcoma
NHL	non-Hodgkin lymphoma
OR	odds ratio
SEER	Surveillance, Epidemiology and End Results

Note: This glossary defines acronyms that occur in more than one summary throughout the Scientific Highlights section.

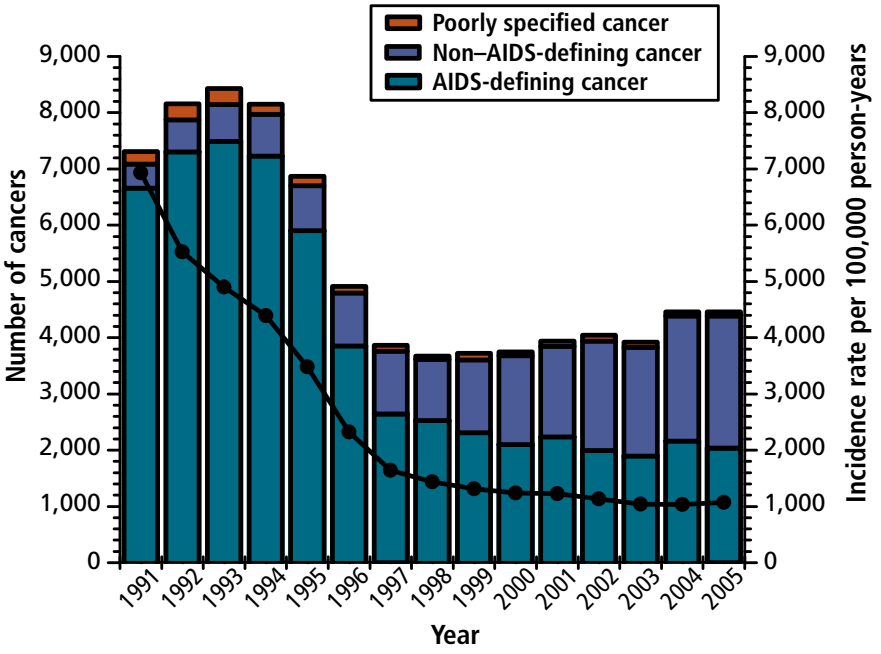


Figure 1. The estimated counts and standardized incidence rates of total cancers among people living with AIDS in the United States stratified by AIDS-defining cancers, non–AIDS-defining cancers, and poorly specified cancers. Bars depict the estimated number of cancers, and points connected by lines depict incidence rates standardized to the 2000 United States AIDS populations by age group, race, and sex. (Shiels MS, et al. *J Natl Cancer Inst* 2011)

cancer risk in Asian and Pacific Islander American (APA) women and to compare its projections to those from NCI's Breast Cancer Risk Assessment Tool (BCRAT). **Methods:** The authors used data from 589 women with breast cancer and 952 women without breast cancer in the Asian American Breast Cancer Study (AABCS) to compute relative and attributable risks. Absolute risks were obtained by combining this information with ethnicity-specific data from SEER and with U.S. ethnicity-specific mortality data to create the AABCS model. Data from the Women's Health Initiative were used to check the calibration and accuracy of the new model. **Results and conclusions:** Relative and attributable risks for APA women were comparable to those in BCRAT; however, the AABCS model usually estimated lower risk projections than BCRAT in Chinese and Filipino women but not in Hawaiian women. The AABCS model was calibrated to ethnicity-specific incidence rates from the SEER program for projecting absolute invasive breast cancer risk and is preferable to BCRAT for counseling APA women. **(Matsuno RK, Costantino JP, Ziegler RG, et al. Projecting individualized absolute invasive breast cancer risk in Asian and Pacific Islander American women. *J Natl Cancer Inst* 2011; May 11 [E-pub ahead of print])**

Breast Cancer Risk Factors and Tumor Subtypes

Purpose: To investigate associations between epidemiological risk factors (age at menarche, parity, age at first full-term birth, family history of breast cancer in first-degree relatives, and current BMI) and tumor subtypes (hormone receptor–positive, hormone receptor–negative, and triple-negative or core basal phenotype [CBP] tumors). **Methods:** Using pooled tumor marker and epidemiological risk factor data from 35,568 invasive breast cancer patients from 34 studies participating in the Breast Cancer Association Consortium, the authors performed case-case and case-control analyses to estimate associations between epidemiological factors and the risk of developing specific tumor subtypes. **Results and conclusions:** Reproductive factors and BMI are most clearly associated with hormone receptor–positive tumors and suggest that triple-negative or CBP tumors may have distinct etiology. **(Yang XR, Chang-Claude J, Goode EL, et al. Associations of breast cancer risk factors with tumor subtypes: A pooled analysis from the Breast Cancer Association Consortium studies. *J Natl Cancer Inst* 2011;103:250–263)**

Diet, Physical Activity, and Prognosis

Purpose: To investigate post-diagnosis diet quality, recreational physical activity, and prognosis among women with breast cancer. **Methods:** The authors evaluated data on 670 women from the Health, Eating, Activity, and Lifestyle Study, a multiethnic prospective cohort study of women with first primary breast cancer. Women completed assessments approximately 6 and 30 months after diagnosis and were followed for 6 years. **Results and conclusions:** Women consuming better quality diets, as defined by higher Healthy Eating Index-2005 scores, had a 60% reduced risk of death from any cause ($HR_{Q4:Q1}$ = 0.40, CI = 0.17–0.94) and an 88% reduced risk of death from breast cancer ($HR_{Q4:Q1}$ = 0.12, CI = 0.02–0.99). Compared with inactive survivors consuming poor-quality diets, survivors engaging in any recreational physical activity and consuming better quality diets had an 89% reduced risk of death from any cause (HR = 0.11, CI = 0.04–0.36) and a 91% reduced risk of death from breast cancer (HR= 0.09,

CI = 0.01–0.89). Associations observed were independent of obesity status. (George SM, Irwin ML, Smith AW, et al. Post-diagnosis diet quality, the combination of diet quality and recreational physical activity, and prognosis after early-stage breast cancer. *Cancer Causes Control* 2011;22:589–598)

CHILDHOOD CANCER

Early Life Radiation and Ultrasounds

Purpose: To examine childhood cancer risks associated with exposure to diagnostic radiation and ultrasound scans *in utero* and in early infancy (ages 0–100 days). **Methods:** The authors used data from the United Kingdom Childhood Cancer Study, including 2,690 childhood cancer cases and 4,858 age-, sex-, and region-matched controls, to estimate risks of all childhood cancers, leukemia, lymphoma, and central nervous system tumors. **Results and conclusions:** There was no evidence of increased risk of childhood cancer with *in utero* exposure to ultrasound scans. After *in utero* exposure to x-rays, non-significant increases in risk for all cancers (OR = 1.14) and leukemia (OR = 1.36) were observed. Exposure to diagnostic x-rays in early infancy was associated with small, non-significant excess risks for all cancers and leukemia, and significant increased risk of lymphoma (OR = 5.14), based on small numbers. The results suggest the need for cautious use of diagnostic radiation imaging procedures to the abdomen/pelvis of the mother during pregnancy and in children at very young ages. (Rajaraman P, Simpson J, Neta G, et al. Early life exposure to diagnostic radiation and ultrasound scans and risk of childhood cancer: Case-control study. *BMJ* 2011;342:d472)

ESOPHAGEAL CANCER

Esophageal Cancer in Young People

Purpose: The authors conducted a retrospective study to better understand the unusual percentage of esophageal cancer (EC) cases in subjects 30 years of age or younger in Western Kenya. **Methods:** The authors abstracted data from the records of 109 young patients diagnosed with EC at Tenwek Hospital in Bomet District, Kenya, from January 1996 through June 2009 and successfully located and interviewed 60 patients or family members to obtain data on clinical course. **Results and conclusions:** The median survival time was 6.14 months, and the most common tumor histology was esophageal squamous cell carcinoma (98%). The male-to-female ratio was 1.4 to 1, and family history was prominent, with 79% reporting a family history of cancer and 43% reporting a family history of EC. (Dawsey SP, Tonui S, Parker RK, et al. Esophageal cancer in young people: A case series of 109 cases and review of the literature. *PLoS Genet* 2010;5:e14080)

GENETICS

Genes and Habitual Caffeine Consumption

Purpose: To search for common genetic variants associated with habitual caffeine consumption, which has been associated with manifold physiologic effects and both detrimental and beneficial health outcomes. **Methods:** The authors performed a meta-analysis of five U.S. genome-wide association studies comprising 47,341 individuals of European descent. Caffeine intake was assessed using semi-quantitative food-frequency questionnaires. **Results and conclusions:** Two loci reached genome-wide significance with no evidence for significant between-study heterogeneity. The strongest associated single nucleotide polymorphism (SNP) (rs4410790) is located at 7p21, upstream of *AHR* (aryl hydrocarbon receptor). The SNP with the second strongest association (rs2470893) mapped to 15q24, between *CYP1A1* and *CYP1A2*. In addition, analyses of 21 candidate genes identified significant gene-based associations between *CYP2C9* and *ADORA2A* and caffeine intake, in addition to *CYP1A2* and *AHR*. Both the *AHR* and *CYP1A2* genes are biologically plausible candidates because *CYP1A2* metabolizes caffeine and *AHR* regulates *CYP1A2*. (Cornelis MC, Monda KL, Yu K, et al. Genome-wide meta-analysis identifies regions on 7p21 [*AHR*] and 15q24 [*CYP1A2*] as determinants of habitual caffeine consumption. *PLoS Genet* 2011;7:e1002033)

Telomere Genes in Familial Cancer

Purpose: The shelterin complex of genes consists of six proteins (ACD, POT1, TERF1, TERF2, TERF2IP, and TINF2) that form telomeres. Mutations in *TINF2* are present in 11%–25% of patients with dyskeratosis congenita (DC), an inherited bone marrow–failure syndrome that puts patients at very high risk of cancer. The authors' objective was to determine whether mutations in five other genes in the shelterin complex are a common cause of DC. **Methods:** The authors evaluated nine classic DC patients and seven patients classified as "DC-like" based on telomere length and other clinical features. None had mutations in any of the known DC genes. The authors conducted sequence analysis of the promoters, exons, and intron-exon boundaries of *ACD, POT1, TERF1, TERF2,* and *TERF2IP*. **Results and conclusions:** Two variants were present in one patient and a healthy parent but absent in 364 controls. Three other variants were rare (< 1%) but present in both patients and controls. These data suggest that except for *TINF2*, mutations in shelterin genes are not a common cause of DC. (Savage SA, Giri N, Jessop L, et al. Sequence analysis of the shelterin telomere protection complex genes in dyskeratosis congenita. *J Med Genet* 2011;48:285–288)

Xeroderma Pigmentosum

Purpose: To determine the frequency of cancer, neurologic degeneration, and mortality in xeroderma pigmentosum

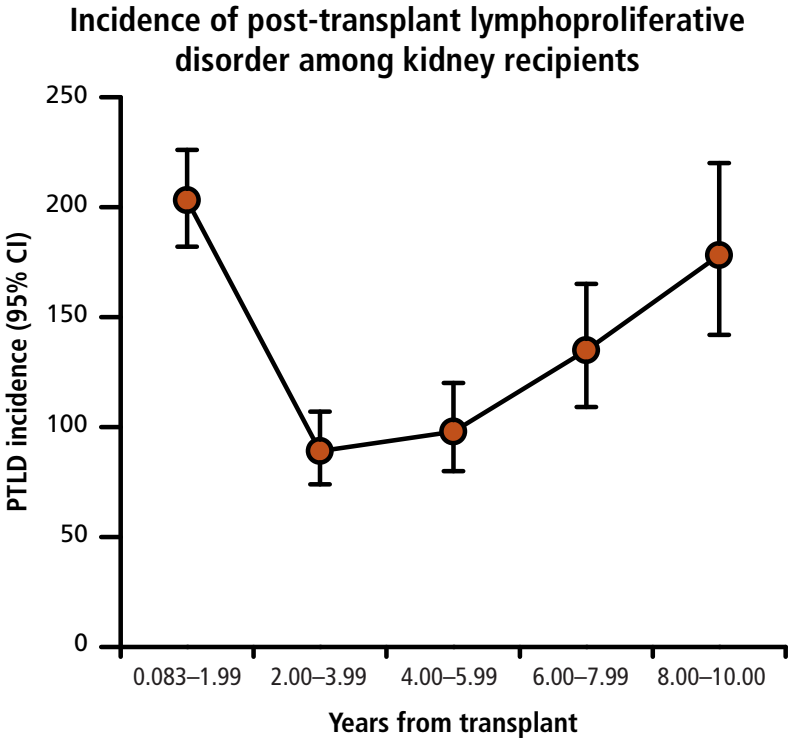


Figure 2. Incidence of post-transplant lymphoproliferative disorder (PTLD) among kidney recipients during 1999–2007. Incidence and 95% CIs are shown as a function of time since transplantation. PTLD incidence is displayed as PTLD events per 100,000 person-years. Follow-up for all recipients began 30 days (0.083 years) after transplantation. (Quinlan SC, et al. *Am J Hematol* 2011)

(XP) patients with defective DNA repair in a 39-year natural history study. **Methods:** All 106 XP patients admitted to NIH from 1971 to 2009 were evaluated from clinical records and follow-up. **Results and conclusions:** The authors observed a 10,000-fold elevation in non-melanoma skin cancer and a more than 2,000-fold increase in melanoma in XP patients under age 20 compared with the U.S. population. The median age at diagnosis of first non-melanoma skin cancer at 9 years (n = 64) was significantly younger than the median age at diagnosis of first melanoma at 22 years (n = 38), suggesting different mechanisms. XP patients with pronounced burning on minimal sun exposure were less likely to develop skin cancer than others, possibly related to extreme sun protection from an early age. Progressive neurologic degeneration was present in 24% (n = 25) with 16 in complementation group XP-D. The most common causes of death were skin cancer (34%), neurologic degeneration (31%), and internal cancer (17%). The median age at death in XP patients with neurodegeneration (29 years) was younger than that in those without neurodegeneration (37 years). The study suggests a major role for DNA repair genes in the etiology of skin cancer and neurologic degeneration. **(Bradford PT, Goldstein AM, Tamura D, et al. Cancer and neurologic degeneration in xeroderma pigmentosum: Long term follow-up characterizes the role of DNA repair. *J Med Genet* 2011;48:168–176)**

LUNG CANCER

Coal and Wood Use in the Home

Purpose: To evaluate the association between in-home solid-fuel use, particularly wood, and lung cancer risk. **Methods:** Using questionnaire data from seven studies in the International Lung Cancer Consortium (5,105 cases and 6,535 controls), the researchers classified subjects as predominant solid-fuel users (e.g., coal, wood) or nonsolid-fuel users (e.g., oil, gas, electricity). **Results and conclusions:** Compared with nonsolid-fuel users, predominant coal users (OR = 1.64), particularly coal users in Asia (OR = 4.93), and predominant wood users in North American and European countries (OR = 1.21) experienced higher risk of lung cancer. The results were similar in never-smoking women and other subgroups. Results are consistent with previous observations relating in-home coal use to lung cancer risk and support the hypothesis of a carcinogenic potential of in-home wood use. **(Hosgood HD III, Boffetta P, Greenland S, et al. In-home coal and wood use and lung cancer risk: A pooled analysis of the International Lung Cancer Consortium. *Environ Health Perspect* 2010;118:1743–1747)**

LYMPHOMA

Lymphoproliferative Disorder After Kidney Transplant

Purpose: To examine differences in risk factors between early onset (i.e., within two years of transplantation) post-transplant lymphoproliferative disorder (PTLD) and late onset (i.e., more than two years after transplantation) PTLD in kidney transplant recipients. **Methods:** The authors conducted a retrospective cohort study using data from the U.S. Scientific Registry of Transplant Recipients. The study included 156,740 kidney transplant recipients, among whom 762 cases of PTLD were diagnosed during follow-up. **Results and conclusions:** There was a "U-shaped" pattern of incidence with time since transplantation, with high PTLD incidence shortly after transplantation, decreasing until two to four years after transplantation, and rising thereafter (see Figure 2). Risk factors for early-onset PTLD included young age at transplantation and Epstein-Barr virus

and cytomegalovirus seronegativity. By comparison, independent risk factors for late-onset PTLD included older age at transplantation and non-Hispanic white race or ethnicity. Steroid maintenance therapy significantly decreased the risk of late-onset PTLD. The bimodal timing and differences in pathology and risk factors suggest that early- and late-onset PTLD are either distinct diseases or a mixture of subtypes with different etiologies. (Quinlan SC, Pfeiffer RM, Morton LM, et al. Risk factors for early-onset and late-onset post-transplant lymphoproliferative disorder in kidney recipients in the United States. *Am J Hematol* 2011;86:206–209)

Trichloroethylene Exposure

Purpose: To investigate the association between NHL and occupational exposure to trichloroethylene (TCE), a chlorinated solvent used for vapor degreasing of metal parts. **Methods:** A total of 1,189 cases and 982 controls provided information on their occupational histories and, for selected occupations, on possible workplace exposure to TCE using job-specific interview modules. An industrial hygienist assessed potential TCE exposure based on this information and a review of the TCE industrial hygiene literature. **Results and conclusions:** NHL was associated with the highest tertiles of estimated average weekly TCE exposure (23 exposed cases; OR = 2.5) and cumulative exposure (24 exposed cases; OR = 2.3, CI = 1.0–5.0) (p for trend = 0.02 and 0.08, respectively). No consistent dose–response relationships across the exposure levels were observed. Overall, neither duration nor intensity of exposure was associated with NHL risk, but the lowest tertile of exposure duration compared with no exposure was related to risk (OR = 2.1, CI = 1.0–4.7). Findings are consistent with an association between high levels of TCE exposure and NHL risk. (Purdue MP, Bakke B, Stewart P, et al. A case-control study of occupational exposure to trichloroethylene and non-Hodgkin lymphoma. *Environ Health Perspect* 2011;119:232–238)

MULTIPLE MYELOMA

Obesity and Myeloma Precursor Risk

Purpose: To assess the role of obesity and race in relation to monoclonal gammopathy of undetermined significance (MGUS), a precursor of multiple myeloma, which has been related to obesity and to higher rates in the black population. **Methods:** The investigators screened 1,000 black and 996 white women aged 40–79 years who were of similar socioeconomic status for MGUS. **Results and conclusions:** A total of 39 (3.9%) blacks and 21 (2.1%) whites had MGUS. Obesity (OR = 1.8), black race (OR = 1.8), and increasing age (older than 55 years vs. younger than 43 years; OR = 2.5) were independently associated with an excess risk of MGUS. Findings support the hypothesis that obesity is etiologically linked to myelomagenesis. The excess of MGUS among blacks compared with whites of similar socioeconomic status supports a role for susceptibility genes in MGUS. (Landgren O, Rajkumar SV, Pfeiffer RM, et al. Obesity is associated with an increased risk of monoclonal gammopathy of undetermined significance among black and white women. *Blood* 2010;116:1056–1059)

RENAL CELL CARCINOMA

Genome-wide Association Study

Purpose: To search for common genetic variants associated with renal cell carcinoma (RCC). **Methods:** The authors conducted a two-stage genome-wide association study of RCC in 3,772 affected individuals and 8,505 controls of European background from 11 studies and followed up 6 single nucleotide polymorphisms (SNPs) in 3 replication studies of 2,198 cases and 4,918 controls. **Results and conclusions:** Two loci on the regions of 2p21 and 11q13.3 were associated with RCC susceptibility below genome-wide significance. Two correlated variants ($r^2 = 0.99$ in controls), rs11894252 and rs7579899, map to *EPAS1* on 2p21, which encodes hypoxia-inducible-factor-2 alpha, a transcription factor previously implicated in RCC. The second locus, rs7105934, at 11q13.3, contains no characterized genes. In addition, the researchers observed a promising association on 12q24.31 for rs4765623, which maps to *SCARB1*, the scavenger receptor class B, member 1 gene. This study reports previously unidentified genomic regions associated with RCC risk that may lead to new etiological insights. (Purdue MP, Johansson M, Zelenika D, et al. Genome-wide association study of renal cell carcinoma identifies two susceptibility loci on 2p21 and 11q13.3. *Nat Genet* 2011;43:60–65)

SECOND CANCERS

Effects of Radiotherapy

Purpose: To estimate the proportion of second cancers attributable to radiotherapy in adults. **Methods:** The authors analyzed 15 cancer sites routinely treated with radiotherapy. The study cohort comprised patients aged 20 years or older and diagnosed with a first primary invasive solid cancer reported to nine SEER registries between 1973 and 2002. **Results and conclusions:** Among 647,672 cancer patients who were 5-year survivors followed up for a mean of 12 years, 60,271 (9%) developed a second solid cancer. For each of the first cancer sites, the relative risk (RR) of developing a second cancer associated with radiotherapy exceeded 1.0 and varied from 1.08 after cancers of the eye and orbit to 1.43 after cancer of the testes. In general, the RR was highest for organs that received more than 5 Gy, decreased with increasing age at diagnosis, and increased with time since diagnosis. The authors estimated that 3,266 excess second solid cancers could be related

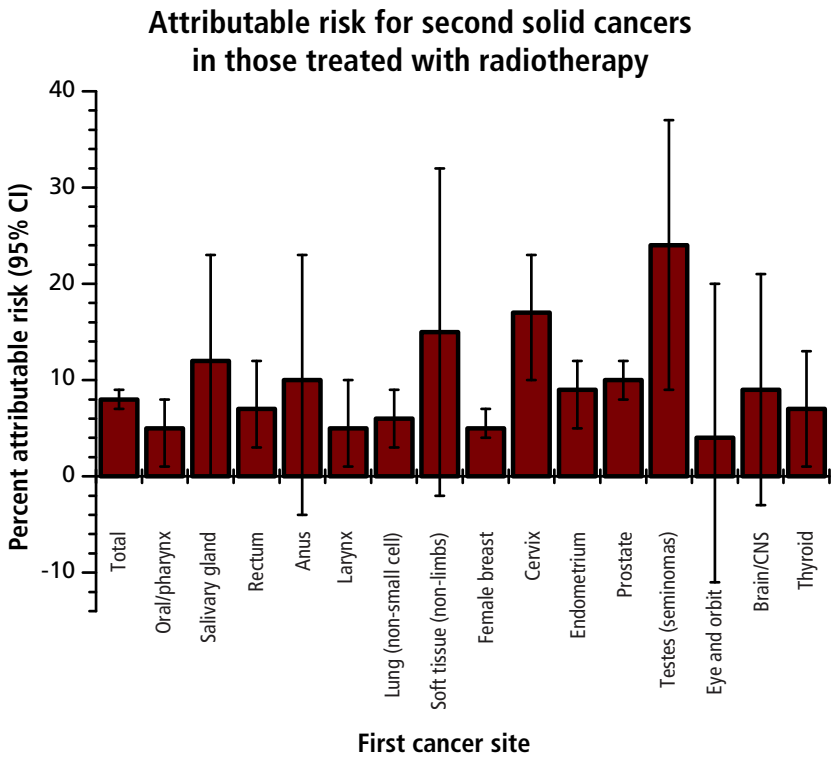


Figure 3. Attributable risk for second solid cancers in patients treated with radiotherapy, arranged by first cancer site. (Figure is based on Table 4 from Berrington de González A, et al. *Lancet Oncol* 2011.)

to radiotherapy, or 8% of the total in all radiotherapy patients surviving at least 1 year, and 5 excess cancers per 1,000 patients treated with radiotherapy by 15 years after diagnosis (see Figure 3). **(Berrington de González A, Curtis RE, Kry SF, et al. Proportion of second cancers attributable to radiotherapy treatment in adults: A cohort study in the U.S. SEER cancer registries. *Lancet Oncol* 2011;12:353–360)**

Risks After Lymphoma Subtypes

Purpose and methods: To evaluate second cancer risks among 43,145 one-year survivors of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), diffuse large B-cell lymphoma (DLBCL), or follicular lymphoma (FL) from 11 SEER population-based registries during 1992–2006. **Results and conclusions:** Among patients without HIV/AIDS-related lymphoma, lung cancer risks were elevated after CLL/SLL and FL but not after DLBCL (standardized incidence ratio [SIR]: CLL/SLL = 1.42, FL = 1.28). A similar pattern was observed for risk of cutaneous melanoma (SIR: CLL/SLL = 1.92, FL = 1.60). Acute non-lymphocytic leukemia risks were significantly elevated after FL and DLBCL, particularly among patients receiving initial chemotherapy, but not after CLL/SLL (SIR: FL = 5.96, DLBCL = 4.96, CLL/SLL = 1.13). Patients with HIV/AIDS-related lymphoma (n = 932) were predominantly diagnosed with DLBCL and had substantially elevated risks for second anal cancer (SIR = 120.50) and KS (SIR = 138.90). These findings suggest that differing immunologic alterations, treatments (e.g., alkylating agent chemotherapy), genetic susceptibilities, and other risk factors (e.g., viral infections, tobacco use) among lymphoma subtypes contribute to the patterns of second malignancy risk. **(Morton LM, Curtis RE, Linet MS, et al. Second malignancy risks after non-Hodgkin's lymphoma and chronic lymphocytic leukemia: Differences by lymphoma subtype. *J Clin Oncol* 2010;28:4935–4944)**

THYROID CANCER

Chernobyl Accident–related Thyroid Cancer in Belarus

Purpose: To evaluate the radiation dose-response for prevalent thyroid cancers diagnosed during the first round of screening in Belarus after the Chernobyl nuclear accident. **Methods:** The authors screened 11,970 individuals aged 18 years or younger at the time of the accident, who had estimated iodine-131 (I-131) thyroid doses based on individual thyroid activity measurements and dosimetric data from questionnaires. The excess OR per gray (EOR/Gy) was modeled using linear and linear-exponential functions. **Results and conclusions:** For thyroid doses less than 5 Gy, the dose-response was linear (n = 85, EOR/Gy = 2.15, CI = 0.81–5.47), but at higher doses, the excess risk fell. The EOR/Gy was increased among those with prior or screening-detected diffuse goiter and was larger (although not statistically significant) for men than women and for persons exposed before age 5 than those exposed between 5 and 18 years. Ten to 15 years after the Chernobyl accident, thyroid cancer risk was increased among individuals exposed to fallout as children or adolescents, but the risk appeared lower than in other Chernobyl studies and studies of childhood external irradiation. **(Zablotska LB, Ron E, Rozhko AV, et al. Thyroid cancer risk in Belarus among children and adolescents exposed to radioiodine after the Chornobyl accident. *Br J Cancer* 2011;104:181–187)**

Chernobyl Accident–related Thyroid Cancer in Ukraine

Purpose: To evaluate the dose-response for Chernobyl accident–related incident thyroid cancers using measurement-based individual I-131 thyroid dose

estimates in a prospective analytic cohort study. **Methods:** The cohort consists of individuals aged less than 18 years on April 26, 1986, who resided in three contaminated oblasts (states) of Ukraine and underwent up to four thyroid-screening examinations between 1998 and 2007 (N = 12,514). I-131 thyroid doses were estimated based on individual radioactivity measurements taken within two months after the accident, environmental transport models, and interview data. **Results and conclusions:** There were 65 incident thyroid cancers diagnosed during the second and fourth screenings and 73,004 person-years of observation. The dose-response was consistent with linearity on relative and absolute scales, although the excess relative risk (ERR) model described data better than the excess absolute risk (EAR) model. The ERR per Gy was 1.91 (CI = 0.43–6.34) and EAR per 10^4 person-years per Gy was 2.21 (CI = 0.04–5.78). The ERR per Gy varied significantly by oblast of residence but not by time since exposure, use of iodine prophylaxis, iodine status, sex, age, or tumor size. I-131–related thyroid cancer risks persisted for two decades following exposure with no evidence of decrease during the observation period. **(Brenner AV, Tronko MD, Hatch M, et al. I-131 dose-response for incident thyroid cancers in Ukraine related to the Chornobyl accident. *Environ Health Perspect* 2011; Mar 14 [E-pub ahead of print])**

Iodine-131 from Nevada Nuclear Bomb Tests

Purpose: To investigate the effects of exposure to radioactive iodine from atmospheric nuclear tests conducted in Nevada in the 1950s. **Methods:** The authors analyzed data on thyroid cancer incidence (18,545 cases) from eight SEER tumor registries for the period 1973–2004. Excess relative risks (ERRs) per Gy for exposure received before age 15 were estimated by relating age-, birth year-, sex-, and county-specific thyroid cancer rates to estimates of cumulative dose to the thyroid that take age into account. **Results and conclusions:** The estimated ERR per Gy for dose received before 1 year of age was 1.8 (CI = 0.5–3.2). There was no evidence that this estimate declined with follow-up time or that risk increased with dose received at ages 1–15. **(Gilbert ES, Huang L, Bouville A, et al. Thyroid cancer rates and ^{131}I doses from Nevada atmospheric nuclear bomb tests: An update. *Radiat Res* 2010;173:659–664)**

Effects of Body Mass Index

Purpose: To clarify the relationship between obesity and thyroid cancer. **Methods:** The researchers examined the association between BMI and thyroid cancer risk in a pooled analysis of five prospective U.S. studies, including 413,979 women and 434,953 men. **Results and conclusions:** Over a mean 10.3 years of follow-up, 768 women and 388 men were diagnosed with thyroid cancer. Risk was greater with increasing BMI per 5 kg/m^2 increase (HR in women = 1.16, HR in men = 1.21, CI = 0.97–1.49). For women and men combined, the HRs for overweight (25.0–29.9 kg/m^2) and obesity (≥ 30 kg/m^2) compared with normal weight (18.5–24.9 kg/m^2) were 1.20 and 1.53, respectively. A significant positive association for BMI in young adulthood (ages 18–20) with thyroid cancer risk was also observed (per 5 kg/m^2 increase: HR = 1.18). **(Kitahara CM, Platz EA, Freeman LE, et al. Obesity and thyroid cancer risk among U.S. men and women: A pooled analysis of five prospective studies. *Cancer Epidemiol Biomarkers Prev* 2011;20:464–472)**

MAJOR EDITORIALS, COMMENTARIES, AND REVIEWS BY DCEG SCIENTISTS

Chanock SJ. A twist on admixture mapping. *Nat Genet* 2011;43:178–179

Chatterjee N, Park JH, Caporaso N, Gail MH. Predicting the future of genetic risk prediction. *Cancer Epidemiol Biomarkers Prev* 2011;20:3–8

Hartge P. Reducing ovarian cancer death rates through screening. *Cancer* 2011;117:449–450

Cardis E, **Hatch M.** The Chernobyl accident—An epidemiological perspective. *Clin Oncol (R Coll Radiol)* 2011;23:251–260

Vlaanderen J, **Lan Q,** Kromhout H, **Rothman N,** et al. Occupational benzene exposure and the risk of lymphoma subtypes: A meta-analysis of cohort studies incorporating three study quality dimensions. *Environ Health Perspect* 2011;119:159–167

Mai PL, Wentzensen N, Greene MH. Challenges related to developing serum-based biomarkers for early ovarian cancer detection. *Cancer Prev Res (Phila)* 2011;4:303–306

Mbulaiteye SM, Goedert JJ. Human herpesvirus 8 seropositivity in rural Uganda: Maturation of sero-epidemiological studies. *J Infect Dis* 2011;203:575–577

Schiffman M. The need for forward-looking decision analyses to guide cervical cancer prevention. *Cancer Epidemiol Biomarkers Prev* 2011;20:219–220

Schiffman M, Wentzensen N, Wacholder S, et al. Human papillomavirus testing in the prevention of cervical cancer. *J Natl Cancer Inst* 2011;103:368–383

Shiels MS, Goedert JJ, Engels EA. Recent trends and future directions in human immunodeficiency virus-associated cancer. *Cancer* 2010;116:5344–5347

Wacholder S, Han SS, Weinberg CR. Inference from a multiplicative model of joint genetic effects for ovarian cancer risk. *J Natl Cancer Inst* 2011;103:82–83

DCEG PEOPLE IN THE NEWS

In February, **Blanche P. Alter, M.D., M.P.H.,** Clinical Genetics Branch (CGB), gave a talk on "Cancer epidemiology" at the Second Meeting for Adults with Fanconi Anemia hosted by the Fanconi Anemia Research Fund in Portland, Oregon. In March, she gave two presentations for the Israel Society of Pediatric Hematology and Oncology in Jerusalem on inherited bone marrow failure syndromes.

In February, **Louise A. Brinton, Ph.D.,** Chief of the Hormonal and Reproductive Epidemiology Branch (HREB), gave a lecture on "Breast cancer risk associated with ovulation stimulation drugs" at a meeting of the European Society of Human Reproduction and Embryology in Kempten, Germany.

In April, several DCEG staff members spoke at the multi-society 2011 Experimental Biology meeting in Washington, D.C. **Carrie R. Daniel, Ph.D., M.P.H.,** Nutritional Epidemiology Branch (NEB), gave a talk titled "Intake of poultry and fish and risk of cancer in the NIH-AARP Diet and Health Study"; **Marianne K. Henderson, M.S.,** Chief of the Office of Division Operations and Analysis, spoke to the American Society for Investigative Pathology on activities of the International Society for Biological and Environmental Repositories; **Alison Mondul, Ph.D.** (NEB), spoke on "Alpha-tocopherol and beta-carotene supplementation and change in circulating VEGF-A, VEGF-C, and VEGF-D concentrations"; and **Stephanie J. Weinstein, Ph.D.** (NEB), gave a presentation on "Serum 25-hydroxyvitamin D and lung cancer risk."

In March, **Eric A. Engels, M.D., M.P.H.,** Infections and Immunoepidemiology Branch (IIB), spoke on "Cancer in people with HIV: Recent trends and prevention opportunities" at the Clinical Care of the Patient with HIV Infection course hosted by the Johns Hopkins University School of Medicine in Baltimore, Maryland. In April, he gave an invited talk on "Non-AIDS-defining cancers" at the HIV Management 2011 course in New York City.

Neal D. Freedman, Ph.D., M.P.H. (NEB), gave a talk in January on "The cancer detectives of Linxian, China" for a Biology Department seminar at Georgetown University in Washington, D.C.

In February, **Gretchen L. Gierach, Ph.D.** (HREB), gave a presentation on "Breast density: Implications for breast cancer etiology" at the University of North Carolina Gillings School of Global Public Health in Chapel Hill.

Ann W. Hsing, Ph.D. (IIB), spoke on "Cancer epidemiology" to students in the Mathematics and Science Academy at the Winston Churchill High School in Potomac, Maryland, in January. She also gave a presentation on "Cancers of the prostate and biliary tract: An epidemiologic journey from China to Africa" at the University of Maryland School of Public Health in College Park in March and spoke on prostate cancer epidemiology at George Washington University in Washington, D.C., in April.

Wen-Yi Huang, Ph.D., M.S.P.H., Occupational and Environmental Epidemiology Branch (OEEB), gave an invited talk on "Utility of biospecimens for epidemiologic research: Experience from the PLCO trial" at the Second Biobanking Conference hosted by the Cambridge Healthtech Institute in Providence, Rhode Island, in December.

In April, **Hormuzd A. Katki, Ph.D.,** Biostatistics Branch (BB), spoke at the Memorial Sloan-Kettering Cancer Center in New York City in its Department of Epidemiology and Biostatistics. His talk was titled "Lessons learned about the value of risk stratification in screening for cervical and lung cancer."

In May, **Stephanie Kovalchik, Ph.D.** (BB), received the Dean's Outstanding Student Award in Biostatistics from the University of California, Los Angeles School of Public Health. This award honors a top graduating student from each department within the school based on scholarship and activities.

In April, **Christian Kratz, M.D.** (CGB), gave a presentation on "The *DICER1* syndrome" at a meeting of the German Working Group on Childhood Human Genetics in Freiburg, Germany.

In February, **Maria Teresa Landi, M.D., Ph.D.,** Genetic Epidemiology Branch (GEB), gave a talk titled "Meta-analysis of lung cancer GWAS" at a meeting of the International Lung Cancer Consortium in Scottsdale, Arizona.

JENNIFER LOUD RECEIVES IRB APPOINTMENT

In March, **Jennifer T. Loud, R.N., C.R.N.P., D.N.P.**, Deputy Chief of the Clinical Genetics Branch, was appointed Vice Chair of the NCI Clinical Center Institutional Review Board (IRB), which reviews NCI protocols for clinical trials and other studies carried out at the NIH Clinical Center. Along with her expertise in clinical cancer genetics, Dr. Loud brings to the position her considerable experience in the complex and rapidly evolving regulatory issues faced by this IRB, on which she has served for approximately three years.

In April, she spoke on "Dietary quercetin and metabolic gene expression in relation to lung cancer risk in the Environment and Genetics in Lung Cancer Etiology (EAGLE) Study" at the Plant Phenolics and Human Health Research Interest Group meeting in Washington, D.C.

Martha S. Linet, M.D., M.P.H., Chief of the Radiation Epidemiology Branch (REB), gave an invited talk on "Cellular telephones, other rapidly changing technologies and cancer risk: Discerning signals amid great noise" at the Division of Environmental Health, Keck School of Medicine, University of Southern California, in Los Angeles in March.

Phuong Mai, M.D., M.S. (CGB), received a first prize travel award in April for her abstract "Confirmation of family history in a population-based survey" in the Epidemiology and Bioinformatics section of the Seventh Annual NCI Retreat for Staff Scientists and Staff Clinicians. On behalf of DCEG, **Martha S. Linet, M.D., M.P.H.,** Chief of REB, offered opening remarks at the retreat along with Lee J. Hellman, M.D., of the NCI Center for Cancer Research (CCR).

In March, **Mary Lou McMaster, M.D., Dilys M. Parry, Ph.D.,** and **Xiaohong (Rose) Yang, Ph.D., M.P.H.,** all of GEB, attended the Third International Chordoma Research Workshop in Bethesda, Maryland. Dr. McMaster presented an "Update on the epidemiology of chordoma: Surveillance Epidemiology and End Results (SEER) registry data 1973–2007." Dr. Parry, a member of the organizing committee, presented a poster titled "Clinical features distinguish childhood chordoma associated with tuberous sclerosis complex from chordoma in the general pediatric population." Dr. Yang gave a talk titled "Identification of a major susceptibility gene, T (brachyury), for familial chordoma using combined linkage and array-CGH approaches."

Mary Lou McMaster, M.D. (GEB), received the Surgeon General's Certificate of Appreciation for "Continued excellence in service as a member of the Public Health Service Ensemble" in November. In March, she attended the Fourth International Patient-Physician Summit on Waldenström's Macroglobulinemia held in Orlando, Florida. At the meeting, she chaired and spoke at the session "Predispositions to Waldenström's macroglobulinemia."

In March, **Lindsay M. Morton, Ph.D.** (REB), spoke on "The evolving risk of

FOUR DCEG FELLOWS DEFEND THEIR DISSERTATIONS

Since February, four DCEG fellows have defended their doctoral dissertations at three leading academic institutions.

In March, **Kathryn Hughes Barry, Ph.D.,** a fellow in the Occupational and Environmental Epidemiology Branch (OEEB), successfully defended her doctoral dissertation at the Yale School of Public Health in New Haven, Connecticut. She conducted the research for her thesis project, "A prospective study of pesticide exposure polymorphisms in DNA repair genes and cancer risk among pesticide applicators in Iowa and North Carolina," under the supervision of **Michael C.R. Alavanja, Dr.P.H.** (OEEB), and **Jay H. Lubin, Ph.D.,** Biostatistics Branch (BB), along with her mentors from Yale, Dr. Xiaomei Ma and Dr. Tongzhang Zheng. Dr. Barry received a grade of "distinguished," the highest category of merit, from two of the three readers who judged her dissertation. She will continue as a postdoctoral fellow in OEEB.

In April, **Julia Ciampa, D.Phil.,** a fellow in BB and the NIH-Oxford-Cambridge Scholars program, successfully defended her doctoral thesis at Oxford University in the United Kingdom. She conducted her doctoral research, titled "Multilocus approaches to the detection of disease susceptibility regions: Methods and applications," under the supervision of **Nilanjan Chatterjee, Ph.D.,** Chief of BB, and Dr. Chris Holmes of Oxford. Part of Dr. Ciampa's thesis was published recently in *Cancer Research* under the title "Large scale exploration of gene-gene interactions in prostate cancer using a multi-stage genome-wide association study." For her course work and research, she was awarded several honors at NIH and Oxford, including the Aon Prize for academic achievement by the Department of Statistics at Oxford. Dr. Ciampa will return soon to the University of Massachusetts Medical School in Worcester to complete her medical degree.

In February, **Cari Meinhold Kitahara, Ph.D.,** Radiation Epidemiology Branch (REB), successfully defended her doctoral dissertation at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. As a predoctoral fellow in DCEG, she conducted research for her thesis project, titled "The association of obesity with thyroid cancer risk and markers of thyroid function," under the joint mentorship of Dr. Elizabeth A. Platz of Johns Hopkins and **Amy Berrington de González, D.Phil.** (REB). Dr. Kitahara will continue as a postdoctoral fellow in DCEG under the mentorship of Dr. Berrington de González to investigate risk factors for thyroid cancer and potential biological mechanisms underlying its association with obesity.

In May, **CDR Claudine M. Samanic, Ph.D.** (OEEB), successfully defended her dissertation at the Johns Hopkins Bloomberg School of Public Health. She based her research for her dissertation, titled "Associations of cigarette smoking and arsenic exposure with *TP53* gene alterations in bladder cancer," on data and tumor tissue from OEEB's New England Bladder Cancer Study, under the mentorship of **Debra T. Silverman, Sc.D., Sc.M.,** Chief of OEEB. A Commander in the U.S. Public Health Service Commissioned Corps, Dr. Samanic will continue to perform research in OEEB.

acute myeloid leukemia following cancer chemotherapy among adults in the United States" at the Fourth International Symposium on Secondary Leukemia and Leukemogenesis in Rome, Italy.

In February, **Ruth M. Pfeiffer, Ph.D.** (BB), gave a talk on "Two criteria for evaluating risk prediction models" at the Department of Mathematics and Statistics at American University in Washington, D.C.

In March, **Susan Privot,** Office of the Director, was appointed protocol coordinator for the NCI Special Studies Institutional Review Board (SSIRB) after serving as executive secretary for the SSIRB for more than 10 years.

In January, **Sharon A. Savage, M.D.** (CGB), spoke on "The consequences of short telomeres: Dyskeratosis congenita and beyond" at Hematology Grand Rounds, Johns Hopkins Hospital, in Baltimore, Maryland. She also gave a presentation on "Understanding Li-Fraumeni syndrome in children and adults" in April at the Georgetown University Lombardi Cancer Center in Washington, D.C.

Sara Schonfeld, Ph.D. (REB), was awarded a Student Travel Scholarship from the Society for Epidemiology Research for travel in June to the Third North American Congress of Epidemiology in Montreal, Canada.

Mark E. Sherman, M.D. (HREB), gave a presentation in February on "Molecular histology: Visualizing the etiology of breast cancer" at the Institute of Cancer Research, Royal Cancer Hospital, in London, United Kingdom. In March, Dr. Sherman was appointed to the Biospecimen Advisory Group of the American Cancer Society, which met in Atlanta, Georgia.

In January, **Jianxin Shi, Ph.D.** (BB), and CCR colleague Jing Huang, Ph.D., received a 2011 NCI Director's Innovation Principal Investigator Award at the NCI Intramural Retreat for their project "Identifying susceptibility loci in *p53* binding regions in lung and breast cancer." In addition, three DCEG fellows received NCI Director's Career Development Awards: **Linda Dong, Ph.D.** (OEEB), for "Urinary metabolomic profiles and the subsequent risk of renal cell cancer"; **Jonathan Hofmann, Ph.D.** (OEEB), for "Evaluating the steroid hormone-related effects of atrazine exposure among farmers"; and **Shih-Wen (Wenny) Lin, Ph.D., M.P.H.** (NEB), for a proposal on "Immunoglobulin gene repertoire and gastric cancer risk."

In March, **Rashmi Sinha, Ph.D.,** Deputy Chief of NEB, led the Diet Working Group at the Asia Cohort Consortium meeting in Orlando, Florida. Also in March, Dr. Sinha gave a talk on "Meat and cancer" and **Philip R. Taylor, M.D., Sc.D.** (GEB), spoke on "Alcohol intake and cancer prevention" for the Nutrition and Cancer Prevention Research Practicum, hosted by the NCI Division of Cancer Prevention and the NIH Clinical Center.

Llewellyn Smith, a senior at Walt Whitman High School in Bethesda, Maryland, and a science intern in HREB, won first place in the Medicine and Health category of the 2011 Montgomery County Science Fair in College Park, Maryland, in March for his project on body mass index and lung cancer risk among never, former, and current smokers in the NIH-AARP Diet and Health Study. Mr. Smith also won awards for this project from the American Physiological Society, the Food and Drug Administration Chapter of Sigma Xi, the U.S. Army Research Office, and the U.S. Public Health Service Commissioned Officers Association as well as an honorable mention from the Washington Statistical Society. His primary mentor was **Gretchen L. Gierach, Ph.D.** (HREB).

Nicolas Wentzensen, M.D., Ph.D. (HREB), gave a talk in January at the University of Wisconsin-Madison titled "From HPV biology to cervical cancer prevention."

In January, **David Wheeler, Ph.D., M.P.H.** (OEEB), presented a poster "Visualizing local model fit in Bayesian regression models using the partitioned deviance information criterion" at the Fourth International Institute of Mathematical Statistics and International Society for Bayesian Analysis Joint Meeting in Park City, Utah.

PHILIP CASTLE RECEIVES AWARD FOR GOVERNMENT SERVICE

In June, Dr. Philip E. Castle, formerly of the Hormonal and Reproductive Epidemiology Branch, received the 2010 Arthur S. Flemming Award for Exceptional Achievement in Federal Government Service. Given by the George Washington University in partnership with the Arthur S. Flemming Awards Commission, the award acknowledges Dr. Castle's contributions to the epidemiology and natural history of the human papillomavirus and cervical cancer. Dr. Castle was among 12 award recipients to be honored.

COMINGS...GOINGS

Mercy Guech-Ongey, Ph.D., left the Infections and Immunoepidemiology Branch (IIB) at the completion of her fellowship to work as an epidemiologist at ICF Macro, an ICF International Company in Calverton, Maryland.


Jason Hoskins

Jason Hoskins, Ph.D., has joined the Laboratory of Translational Genomics as a postdoctoral fellow after receiving his Ph.D. in biochemistry from the University of Rochester in New York. His thesis explored the RNA-based mechanism of toxicity caused by the chemotherapeutic drug 5-fluorouracil in *Saccharomyces cerevisiae*. With **Laufey Amundadottir, Ph.D.,** Dr. Hoskins will study the molecular mechanism by which common risk variants on chromosome 13q22 confer susceptibility to pancreatic cancer.

JAY LUBIN, RENOWNED STATISTICIAN, RETIRES

Jay H. Lubin, Ph.D., senior investigator in the Biostatistics Branch, retired in May after serving 33 years at NCI. After receiving a Ph.D. in biostatistics from the University of Washington in 1978, Dr. Lubin joined NCI as a health statistician in what eventually became the Biostatistics Branch of DCEG. Throughout his career, Dr. Lubin has been in tremendous demand for his expertise in the development of statistical methods for designing and analyzing complex epidemiologic studies. In particular, he was a driving force in a series of seminal investigations that have elucidated the effects of tobacco, radon, arsenic, pesticides, and other environmental exposures on the incidence of lung cancer and other malignancies. His impact on statistical and epidemiological research has had an effect both nationally and internationally, leading to significant advances in cancer risk assessment, public health, and public policy.


Stephanie Kovalchik

Stephanie Kovalchik, Ph.D., joined the Biostatistics Branch as a postdoctoral fellow. She received a Ph.D. in biostatistics from the University of California, Los Angeles. Dr. Kovalchik's doctoral dissertation involved statistical issues in estimating treatment and patient factor interactions with meta-analysis. She will be working under the mentorship of **Hormuzd A. Katki, Ph.D.,** and **Ruth M. Pfeiffer, Ph.D.,** on developing absolute risk prediction models and other issues in clinical epidemiology.

Rashida Williams left the Administrative Resource Center in March after six years of service as an administrative technician. She will reside in Florida.

Kelly J. Yu, M.P.H., left IIB at the completion of her fellowship to join the NCI Early Detection Research Network in the Division of Cancer Prevention.

BENCH-TO-BEDSIDE AWARD FEATURES LI-FRAUMENI SYNDROME

Congratulations to **Sharon A. Savage, M.D.,** Clinical Genetics Branch (CGB), who received an NIH Bench-to-Bedside Award for her project "Mitochondria, telomeres, and lifestyle in Li-Fraumeni syndrome outcomes." Dr. Savage's collaborators are Dr. Maria Isabel Waddington Achatz of São Paulo, Brazil; **Mark H. Greene, M.D.**, Chief of CGB; Dr. Pierre Hainaut of the International Agency for Research on Cancer (IARC) in Lyon, France; Paul M. Hwang, M.D., Ph.D., with the National Heart, Lung, and Blood Institute (NHLBI) of NIH; **Phuong Mai, M.D., M.S.** (CGB); Dr. David Malkin from the University of Toronto in Ontario, Canada; **Charles Matthews, Ph.D.,** Nutritional Epidemiology Branch (NEB); **Rashmi Sinha, Ph.D.,** Deputy Chief of NEB; **Ingrid Wentzensen, M.D.** (CGB); and **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG.

Li-Fraumeni syndrome (LFS) is a rare, inherited disorder that predisposes young people to multiple forms of cancer, most notably breast cancer, sarcomas, brain tumors, and adrenocortical tumors. LFS is characterized by germline mutations in the *p53* tumor suppressor gene, which occur in approximately 70 percent of patients diagnosed with LFS. The proposed study is a collaborative effort involving NCI, NHLBI, and other centers in Brazil, Canada, and the United States. The initial studies will include an evaluation of the contribution of germline *TP53* mutations to mitochondrial function and an assessment of these mutations as a potential metabolic biomarker of cancer risk as well as an investigation of the role of telomere biology as a cancer risk modifier. In addition, a pilot study collecting data on diet, physical activity, and other risk factors will be conducted as a first step toward an intervention study.

The NIH Bench-to-Bedside Award Program fosters collaborations among laboratory, clinical, and population scientists in efforts to improve the understanding of important disease processes that may lead to new therapeutic, preventive, or diagnostic interventions.

A TRIBUTE TO ARTHUR SCHATZKIN

Arthur Schatzkin, M.D., Dr.P.H., passed away on January 20 from cancer. An internationally renowned pioneer in the field of nutrition and cancer, Dr. Schatzkin joined NCI in 1984 and became the Chief of the Nutritional Epidemiology Branch (NEB) in 1995.

With a publication record surpassing 400 original research articles, Dr. Schatzkin was committed to understanding the role of nutrition in cancer etiology and prevention. Early in his career, he was the first to describe an association between moderate alcohol intake and breast cancer risk. He then turned his attention to the role of diet in preventing colorectal cancer, leading to the landmark NCI Polyp Prevention Trial.

Dr. Schatzkin was instrumental in addressing the major methodological issues that have impeded progress in nutritional epidemiology. As an example, to overcome the limited range of reported dietary intake in cohort studies, he conceived and launched the NIH-AARP Diet and Health Study, which at the time was the largest prospective cohort investigation of diet and nutrition in relation to cancer causation. This long-term study of approximately 500,000 men and women already has generated more than 100 original scientific papers and continues to be an invaluable resource utilized by investigators worldwide. "I have always considered Arthur to be the most brilliant cancer prevention researcher in the U.S. and, at the same time, a wonderful friend to literally thousands of us in academia and beyond," commented Dr. David S. Alberts, Director of the Arizona Cancer Center at the University of Arizona in Tucson.

During Dr. Schatzkin's tenure as Branch Chief, NEB grew from two investigators to a highly productive team of more than 20 scientists. He was dedicated to the pursuit of strategies in nutritional epidemiology and to the training, mentoring, and support of young scientists. "The family-friendly atmosphere that he fostered in the Branch was crucial for me in achieving work/life balance," said **Stephanie J. Weinstein, Ph.D.,** a staff scientist. According to **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, "Arthur Schatzkin was at the forefront of efforts to meet the challenges of research

Arthur Schatzkin

in nutritional epidemiology, developing new methods to assess the components of nutritional status, and providing leadership that inspired creativity and passion in trainees and senior scientists alike. He had great personal warmth, intellectual curiosity, and a genuine commitment to improve public health through exemplary science."

Finally, **Amanda J. Cross, Ph.D.,** a tenure-track investigator in NEB, commented, "His legacy lives on through those of us who admired and looked up to him as an extraordinary mentor and role model who blazed new trails for us to follow." ■

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