Division of Cancer Epidemiology and Genetics

DCEG

Linkage

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IN THIS ISSUE:

NATIONAL CANCER INSTITUTE

DCEG MOVES AHEAD WITH BLADDER CANCER RESEARCH

The DCEG is conducting two complex, state-of-the-art studies—one in Spain, the other in New England—to clarify the causes of bladder cancer. Epidemiologic studies have pointed to tobacco use and certain occupational exposures as key risk factors. Although these exposures probably account for a large proportion of bladder cancer cases, the roles of other possible factors such as fluid intake, nutrition, infection, and potential effect modifiers such as genetic polymorphisms, urine pH, and urinary frequency are poorly understood.

Map of Spain showing the five recruitment areas for the Bladder Cancer Study: Alicante, Barcelona and Valley-Occidental, Oviedo, Tenerife.

Occupational Epidemiology Branch (OEB) researchers **Mustafa Dosemeci, Ph.D., Debra Silverman, Sc.D.,** and **Nathaniel Rothman, M.D.**, launched an interdisciplinary case-control study of bladder cancer in Spain. This extensive study was done in collaboration with Spanish researchers Drs. Manolis Kogevinas, Núria Malats, Paco Real, and Adonina Tardón. Other DCEG investigators included **Claudine Samanic, Montserrat Garcia-Closas, Kenneth Cantor, Patricia Stewart, Juan Alguacil,** and **Roel Vermeulen**.

The study of 1,233 cases and 1,295 controls is one of the largest to focus on occupational exposures and bladder cancer risk. A series of 63 occupational modules was developed to obtain extensive exposure information on study participants. Data collection, using a computer-assisted personal interview system, finished in June 2001. The interviews took on average 80 minutes to complete, with the occupational portion accounting for nearly half of that time.

Although Spain and the U.S. have similar incidence rates of bladder cancer, some exposures linked to bladder cancer are more prevalent in Spain. For example, in the 1970's, the U.S. banned the use of aromatic amines, which were frequently used in textile dyeing and rubber manufacturing and were shown to be carcinogenic to the bladder. However, aromatic amines were still used in Spain in the 1990's. The use of diesel fuel, another suspected bladder carcinogen, is also much higher in Spain than in the U.S.

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According to Dr. Dosemeci, differential occupational exposure was one reason Spain was an ideal place to conduct the study. He also noted that people were willing to participate; researchers obtained a response rate of 86 percent for the interview, and 94 percent of participants in the case group gave biospecimens.

The biospecimens will be used to study gene-environment interactions and, more specifically, threshold doses of exposure leading to DNA damage. Dr. Dosemeci anticipates that genotyping will be completed in 2003, as well as initial data analysis of the main effects of potential risk factors.

In New England, elevations in bladder cancer mortality rates have been observed among men and women over the past 30 years, based on the cancer maps produced by DCEG staff. Early research suggested these elevations might be caused by exposures in the textile and leather industries, but the rates failed to decline after these industries left the region. The persistently high rates intrigued Dr. Silverman and another OEB researcher, **Dalsu Baris, M.D., Ph.D.**, and led them to launch the New England Study of Environmental Health. The study is underway in New Hampshire, Vermont, and Maine, and it aims to recruit 1,200 cases and 1,200 controls.

The research focuses on the carcinogenic effects of drinking water contaminants, primarily inorganic arsenic. Studies in other parts of the world show an increased risk of bladder cancer associated with high levels of inorganic arsenic in drinking water. However, the risks associated with low-to-moderate exposure—levels thought to occur in water drawn from private wells in the New England region—are less clear. Private wells serve as the source of drinking water for nearly 40 percent of people living in the study region, compared to 5 to 20 percent of the total U.S. population.

The New England study will explore other risk factors such as smoking, occupational exposures, dietary factors, prior and current medical conditions, drug use, hair dye use, and urinary tract infections. The role of effect modifiers such as urinary stasis, urine pH, and susceptibility genes such as *NAT2*, *GSTM1*, and those encoding cytochrome p450 enzymes will also be examined. Etiologic leads generated from the Spanish study will also be examined in New England.

Studies in other parts of the world show an increased risk of bladder cancer associated with high levels of inorganic arsenic in drinking water. However, the risks associated with low-to-moderate exposure—levels thought to occur in water drawn from private wells in the New England region—are less clear.

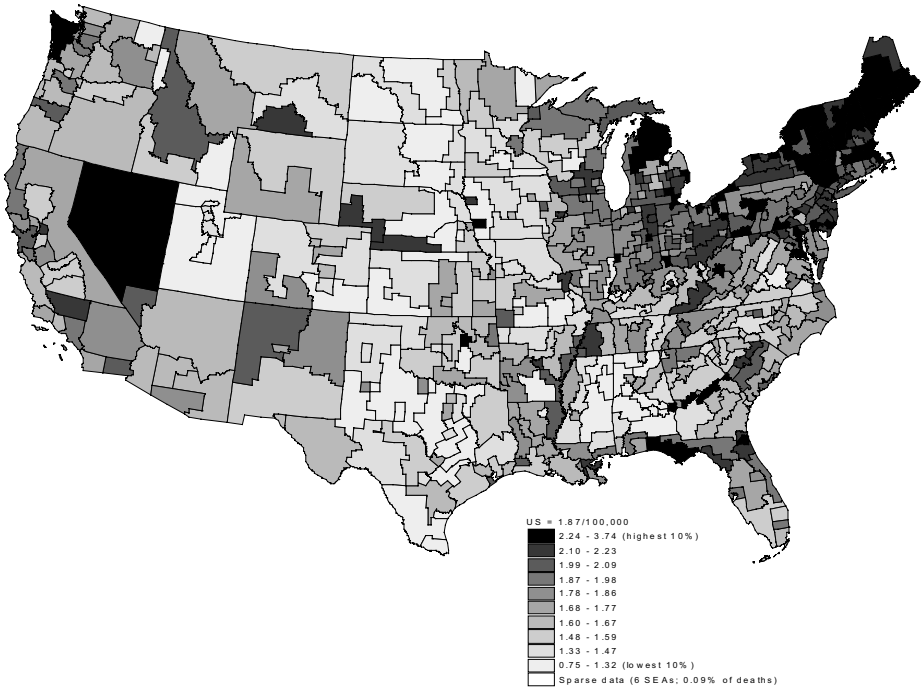
Like the Spanish study, participants in the New England study are being asked to provide information during a computer-assisted personal interview carried out in their homes by trained interviewers. During the interview, drinking water samples and biological specimens including toenails (for measuring arsenic levels), buccal cells and blood (for DNA and other biomarkers), and urine (for arsenic metabolites and pH) will be collected.

A distinctive feature of the New England study involves the use of global positioning system receivers to determine latitude and longitude of current residences. Coupled with geographic information system (GIS) technology, this information will allow for a more detailed analysis of proximity to hazardous waste sites and industries than previously possible, and the researchers will obtain better estimates of potential exposures from contaminant releases. OEB researchers **Mary Ward, Ph.D.** and **Jay Nuckols, Ph.D.** are lead investigators on the study's GIS component.

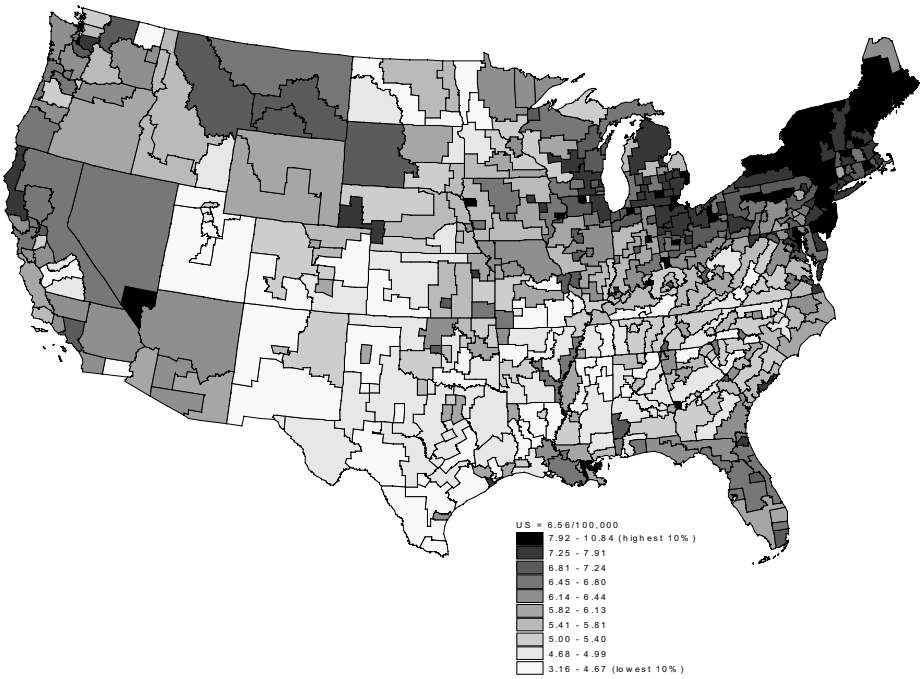
Along with Drs. Baris and Silverman, the DCEG team includes OEB researchers Kenneth Cantor, Ph.D., who directs the water component and Nathaniel Rothman, M.D., M.P.H., who leads the biological component of the study. On-site collaborators include Drs. Margaret Karagas and Richard Waddell (Dartmouth Medical School), Dr. Margaret Parsons (Maine Bureau of Public Health), Jennifer Taylor (New Hampshire Department of Health and Human Services), and Dr. Burton Wilcke (Vermont Department of Health). Joseph Ayotte, of the U.S. Geological Survey will collaborate closely on the exposure assessment of arsenic for each study participant. ■

—Maria Sgambati, M.D.

Cancer Mortality Rates by State Economic Area (Age-adjusted 1970 US Population) Bladder: White Females, 1970–94



Cancer Mortality Rates by State Economic Area (Age-adjusted 1970 US Population) Bladder: White Males, 1970–94



RENAL CANCER STUDY SEEKS TO UNDERSTAND ETHNIC DIFFERENCES IN INCIDENCE RATES

For the past two decades, the incidence and mortality rates for renal cell cancer have been on the rise, with more rapid increases noted among African Americans than Caucasians. However, the reasons behind the upward trend and the ethnic differences remain unclear. In April, **Wong-Ho Chow, Ph.D.**, and **Joanne Colt, M.P.H., M.S.**, of the Occupational Epidemiology Branch, launched the "Case-control Study of Renal Cell Cancer Among Caucasians and African Americans in the U.S." This population-based study will strive to identify environmental and genetic determinants that underlie the demographic patterns. In particular, the investigators hope to clarify the role of smoking, obesity, hypertension, medications, and susceptibility genes in the etiology of renal cancer.

Dr. Chow and Ms. Colt, along with colleagues Dr. Kendra Schwartz (Wayne State University) and Dr. Faith Davis (University of Illinois), plan to recruit 1,400 Caucasian and 700 African American cases and 2,800 controls from the Detroit and Chicago metropolitan regions over a four-year period. Participants will complete a 90-minute interview and provide samples of saliva and blood.

Because response rates have generally declined for epidemiologic research, the researchers have made special efforts to maximize recruitment. Focus groups, held in Chicago and Detroit, helped identify barriers and effective incentives to participation. Concern was expressed that biospecimen collections may deter some potential interviewees and thereby reduce response rates. As part of the study, different recruitment methods will be evaluated to better understand the reasons behind decisions to participate (or not) in a research project.

The investigators also learned that extensive promotional efforts would be needed to familiarize people with the study and to obtain their trust before contacting them to participate. About 15 community groups in each city have agreed to serve as "Ambassadors" to spread the word about the study, including the Detroit Urban League, the National Black Leadership Initiative on Cancer in Chicago, local health departments in the affected counties, the Cancer Information Service, and the Kidney Cancer Association. The Ambassadors have received careful training and are now disseminating brochures and posters in health fairs, senior citizen centers, supermarkets, and other places. A media campaign targeting local newspapers, radio stations, and TV stations is also underway.

"We have been conducting renal cancer studies for many years now," said Dr. Chow, "and we have some clues to lifestyle factors, but we have not looked in detail at genetic factors. We hope to do so in this study. Very little is known about the risk factors for African Americans, and we hope to find out why they have higher rates for these tumors." ■

—Joanne Colt, M.P.H., M.S.

DCEG DIRECTOR JOSEPH FRAUMENI ELECTED TO NATIONAL ACADEMY OF SCIENCES

In April, **Joseph F. Fraumeni, Jr., M.D.**, was elected to membership in the National Academy of Sciences (NAS). Election to the NAS is one of the highest honors bestowed in science, recognizing individuals for their past and ongoing achievements in original research. Dr. Fraumeni joins 71 other U.S. scientists and engineers elected this year as well as 15 foreign associates from 12 countries. Two other NIH scientists, Dr. Harvey Alter from the Division of Transfusion Medicine at the NIH Clinical Center, and Dr. Adriaan Bax from the National Institute of Diabetes and Digestive and Kidney Diseases, also were elected this year.

The NAS was established in 1863 by a congressional act signed by Abraham Lincoln. As a private organization of scientists and engineers dedicated to furthering science, the NAS advises the federal government on scientific and technical matters. Following this year's election, NAS now has 1,907 members in the United States and 330 foreign associates.

Dr. Joseph F. Fraumeni, Jr.

DCEG MOURNS LOSS OF DR. TERRY THOMAS

Terry Thomas, Ph.D., a senior staff scientist in the Radiation Epidemiology Branch and a leading contributor to studies of radiation health effects in the former Soviet Union, died of cancer on March 3 at her home in Silver Spring.

Dr. Thomas is remembered for her "natural talent for epidemiology and her deep commitment to public health," said Joseph Fraumeni, Jr., M.D., DCEG Director. "She became a scientific ambassador for NIH over the past few years, working closely with a variety of scientists from several countries on a very complex epidemiological investigation into the Chornobyl disaster. She renewed and invigorated the project at a critically important time, and we are deeply indebted to her."

Dr. Thomas began her career at NCI in 1971, shortly after graduating from the University of Colorado in Boulder with a degree in sociology. While employed as a statistical assistant in NCI's Epidemiology Branch, she went on to obtain a masters degree in biostatistics at Georgetown University in 1977 and a doctoral degree in occupational health from Johns Hopkins University in 1986.

"She had a lot of drive," said Gilbert Beebe, Ph.D., NCI Scientist Emeritus. "She was a very determined lady and an incredible worker."

Dr. Thomas' early NCI research focused on occupational cancer, particularly brain cancer among petrochemical workers and lung cancer related to silica and talc exposure. "Those were the early days of trying to incorporate industrial hygiene into epidemiological studies," said Robert Hoover, M.D., Sc.D., Director of NCI's Epidemiology and Biostatistics Program. "Terry was one of the pioneers in integrating better measurements of what people were exposed to on the job. She was tenacious, combining sound epidemiology skills with the ability to work with a variety of people to get the job done."

In 1987, Thomas left NCI to join the Department of Veterans Affairs, where she studied the effects of Agent Orange on Vietnam War veterans. Four years later, she joined the Department of Energy and began research on the 1986 Chornobyl nuclear disaster in the former Soviet Union.

"Throughout her career, Terry had a propensity for taking on epidemiology where it's not so easy to do—in submarines and Chornobyl," said Patricia Hartge, Sc.D., NCI Deputy Director of the Epidemiology and Biostatistics Program. "If the answers demanded you go to the ends of the earth and be uncomfortable getting there, she'd do it. She was profoundly interested in getting answers in a practical and careful way."

Dr. Thomas continued to explore the effects of radiation throughout her career, joining several international study groups researching occupational and radiation health issues.

That interest brought her back to NCI in 1999, where she played a vital leadership role in reshaping NCI's Collaborative Chornobyl Research Program.

"Dr. Thomas traveled extensively, investigating leukemia among the men tasked with cleaning up Chornobyl and thyroid cancer among children," Dr. Beebe said. "She worked overseas with such spirit; she will be tremendously missed by her many friends and colleagues in Russia, Belarus, and Ukraine. She contributed so much to the program."

Dr. Thomas was also a dedicated educator. From 1994 to 1999, she was an associate professor and division director at the Uniformed Services University of the Health Sciences in Bethesda. While there she conducted research on the health of persons assigned to submarines. Dr. Thomas also taught courses at George Washington University and Georgetown University.

Dr. Terry Thomas

"Throughout her career, Terry had a propensity for taking on epidemiology where it's not so easy to do—in submarines and Chornobyl."

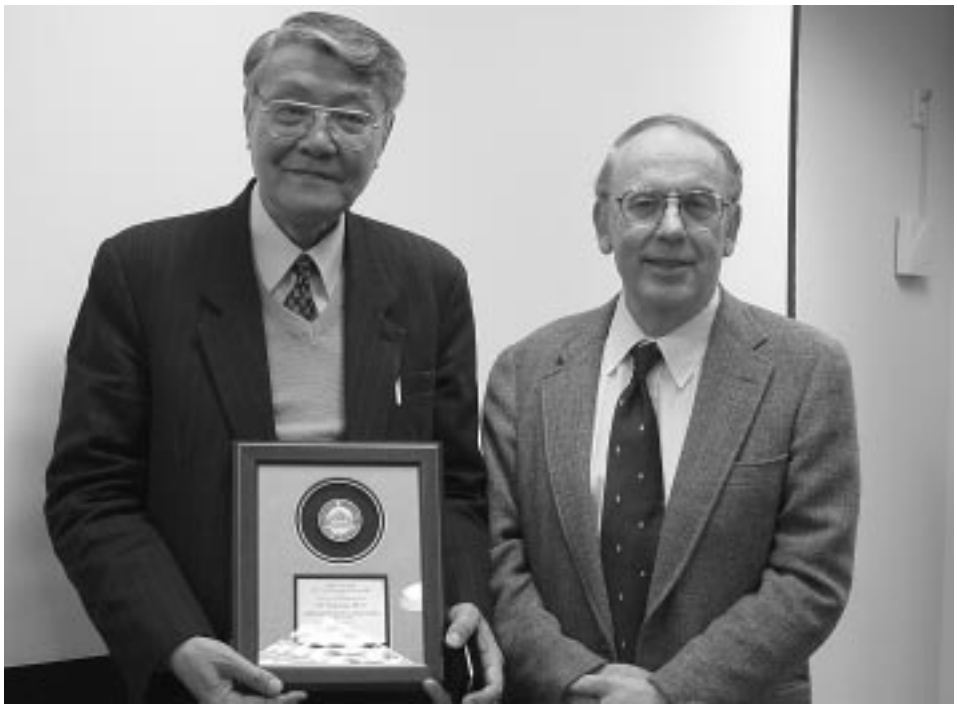
"Terry loved epidemiology, and she communicated that enthusiasm to her students," said her husband, Dr. Mike Radtke, of the NIH Center for Scientific Review. "Just days before she died, she was signing off on the thesis cover sheets sent to her by her students. She worked right up until the end. If she said she'd do something, she got it done."

Dr. Thomas authored or co-authored more than 30 peer-reviewed journal articles. She was a Fellow of the American College of Epidemiology. Her private pursuits included travel, gourmet food, gardening, and aerobic exercise. She was an aerobics instructor for more than a decade and walked the 60-mile Avon Breast Cancer Three-Day Walk in 2000. ■

—Kathleen Stine, M.B.A.

MARKING 20 YEARS OF COLLABORATION BETWEEN THE NCI AND SHANGHAI CANCER INSTITUTE

***Yu-Tang Gao, M.D.**, and **Enju Liu, M.D.**, of the Shanghai Cancer Institute (SCI) arrived in March for a visit of several months to collaborate with **Dr. Ann Hsing** and others on analyses of the Shanghai Biliary Tract Cancer Study. During his visit, Dr. Gao gave a DCEG seminar on 20 years of collaboration between the NCI and the SCI.*



Drs. Yu-Tang Gao and Joseph F. Fraumeni, Jr.

In the 1970's, new relations between the United States and China led to a formal research agreement involving the NIH and the Chinese Ministry of Public Health. From that agreement, NCI and the Shanghai Cancer Institute (SCI) forged a collaboration that celebrates its 20th anniversary this year. Dr. Yu-Tang Gao, a founder of the collaboration, recently reflected on two decades of work between the groups at a DCEG seminar. DCEG Director **Dr. Joseph Fraumeni** marked the event by presenting Dr. Gao with an NCI keepsake and a plaque recognizing his "monumental contributions to cancer epidemiology."

During two decades of major collaboration, several major population case-control studies were carried out in China for cancers of the lung, gastrointestinal system, prostate, and biliary tract. The collaboration also produced numerous publications on cancer incidence trends by tumor site, and on a variety of case-control and cohort studies that provided new insights into cancer etiology. Many scientists have contributed to this diverse group of projects. Dr. Gao credits superb research teams at NCI and SCI, including Drs. William Blot (formerly of the NCI) and **Susan Devesa** (Biostatistics Branch), **Wong-Ho Chow** [Occupational Epidemiology Branch (OEB)], Joseph Fraumeni (OD), and Ann Hsing (Environmental Epidemiology Branch); Drs. Bing Li and Jun Yao Li of the Chinese Academy of Medical Sciences; Dr. Tian Gen Wang of the Beijing Medical University; and Dr. Bao Zhen Wu of the Chinese (Union) Medical University.

Working with Drs. Blot and Fraumeni of NCI and Dr. Chang-Wen Hsu of SCI, one of Dr. Gao's first tasks was to determine why Shanghai had such high lung cancer incidence and mortality rates, particularly in women. Their case-control studies implicated not only smoking, but also exposures to volatile emissions from unrefined cooking oils, which become mutagenic when heated. The group published more than a dozen articles that helped identify specific lung carcinogens in the cooking oil volatiles, and described other risk factors, including occupational exposures and pre-existing infections such as tuberculosis.

During two decades of major collaboration, several major population case-control studies were carried out in China for cancers of the lung, gastrointestinal system, prostate, and biliary tracts… [as well as] cohort studies that [have] provided new insights into cancer etiology.

In the late 1980's and early 1990's, Dr. Devesa helped carry out work on Shanghai cancer incidence patterns. This work identified changing cancer patterns in China, notably a dramatic increase in cancers of the biliary tract, and decreases in esophageal and gastric cancers. From these findings, Dr. Hsing and Drs. Gao, Deng, Ming-Chang Shen, and Bing-Sheng Wang, planned and conducted a population-based case-


Shanghai Cancer Institute

control study of biliary tract cancers. This was the most comprehensive study of biliary cancer ever undertaken; in 2001 it completed enrollment of 710 cases, 1,060 gallstone patients, and 999 controls. Data analyses from this study are now yielding clues to the role of various lifestyle factors, medical conditions, and genetic mechanisms.

The descriptive studies also revealed an increasing trend for prostate cancer, despite very low background rates, which paved the way for a case-control study. The study completed enrollment in 1995 and has explored several hypotheses, including factors related to 'westernization' such as low intake of protective factors (soy, antioxidants), high intake of potential carcinogens (meat, animal products), obesity, and physical inactivity.

One of the most ambitious activities to arise from the NCI-SCI collaboration is the Shanghai Women's Study, being carried out in conjunction with Vanderbilt University. The study aims to enroll 75,000 women in a prospective cohort to determine environmental and genetic risk factors for cancer among Chinese women. Playing key roles are DCEG investigators Drs. Chow and **Nathaniel Rothman** (OEB), and SCI researcher Dr. Fan Jin. A pilot study is underway to determine the feasibility of carrying out a similar study of men.

"The unique exposures, unique cancer patterns, and feasibility of conducting population-based research in Shanghai have created a favorable collaborative climate," Dr. Gao concluded. ■

—Maria Sgambati, M.D.

GENE-ENVIRONMENT INTERACTIONS ARE FOCUS OF CHILDHOOD CANCER MEETING

More than 100 researchers from around the world gathered on March 25-26 in Bethesda, MD, for the Workshop on Gene-Environment Interactions in the Etiology of Childhood Cancer. The meeting was sponsored by the NCI Office of the Director as well as four NCI Divisions: the DCEG, the Center for Cancer Research, the Division of Cancer Control and Population Sciences, and the Division of Cancer Treatment and Diagnosis. Chaired by DCEG scientist **Martha Linet, M.D.**, the meeting brought together a multidisciplinary group of scientists to assess the state of knowledge in etiologic studies of childhood cancer, identify gaps in understanding, and highlight promising research areas. In an opening address, Alfred Knudson, M.D., Ph.D., of the Fox Chase Cancer Center, discussed interrelationships among studies of genes, environment, and populations in understanding childhood cancers.


Dr. Martha Linet addresses Childhood Cancer Meeting

An important emphasis of the proposed workshop was to bridge conceptual and operational gaps between hypothesis-generating epidemiological studies and laboratory studies to identify and facilitate possible synergies between epidemiologic, genetic, and animal model researchers. To carry this out, the workshop was divided into three panels: lifestyle factors including nutrition, diet, parental smoking and alcohol consumption, and physical activity; exposures from parental occupations, environmental sources, and medical interventions; and the role of infectious diseases and immune function.

DCEG scientist emeritus **Robert W. Miller, M.D., Dr.P.H.**, addressed the group on the closing day of the workshop and was honored for his enduring contributions to epidemiologic and etiologic studies of childhood cancer.

KNIGHT JOURNALISM FELLOW RITA RUBIN VISITS DCEG

In March, DCEG was privileged to serve as a host for Knight Medical Science Journalism Fellow, Ms. Rita Rubin. Ms. Rubin is a health reporter for *USA Today* and has spent nearly 25 years in journalism covering various topics for *US News and World Report*, *The Dallas Morning News*, and the *Columbus Citizen-Journal*.

DCEG staff had the chance to learn about the story-making process in scientific reporting through an informal seminar given by Ms. Rubin. Her presentation, "Headlines, Deadlines, Bylines, and Storylines: Chatting with USA Today Reporter Rita Rubin," highlighted the evolution of a topic from an idea into a full article, using that day's story as a case study.

"Typically, I am working on at least three stories at any one time, five if I'm nuts," says Ms. Rubin. Each story takes about a week to complete, and final placement within the paper is at the mercy of the editor and the news of the day. Not all of Ms. Rubin's topics are assigned. She uses her judgment to proceed with newsworthy ideas from reliable sources. When researching potential articles, she finds that press materials or information accessible on the Internet are key resources. However, an interview is sometimes critical to finishing a story.

Ms. Rita Rubin

Ms. Rubin understands the skepticism scientists have when talking to the press. "But we're not scientists," she says. "We're journalists and need help. Reporters really want to get it right."

The Knight Center for Specialized Journalism, organized through the Philip Merrill College of Journalism at the University of Maryland, provides opportunities for journalists to pursue their interests at NIH through fellowships and seminars on a variety of topics throughout the year. NIH offers fellows a three-week rotation within the Institutes, which allows health reporters to spend time with scientists and learn more about their fields of research. The goal of the program is "to foster a depth of perception on the part of the writer that translates into better coverage and better information provided to the public," says Carol Horner, director of the Knight Center. "That's the bottom line."

Having reporters spend time at NIH is mutually beneficial. In addition to helping the reporters by giving them tours of the facilities and one-on-one time with the researchers, scientists also learn about the reporter's perspective on a story and its development. ■

—Alyssa Voss

ASPO AND HARVARD RECOGNIZE DR. ROBERT HOOVER FOR RESEARCH CONTRIBUTIONS

Dr. Robert N. Hoover

Robert Hoover, M.D., Sc.D., was awarded the 2002 American Society of Preventive Oncology (ASPO) Distinguished Achievement Award and the 2002 Harvard School of Public Health Alumni Award of Merit. ASPO recognized Dr. Hoover for pioneering research in identifying environmental and hormonal determinants of cancer and for his enduring contributions to epidemiology and public health. Following receipt of the award at the 26th annual ASPO meeting held March 11, 2002, in Bethesda, he addressed the audience on "Etiologic Support for Prevention Efforts—How Deep Should It Be?" The Harvard School of Public Health, where Dr. Hoover received his doctorate in epidemiology in 1976, recognized him for outstanding contributions to the field of public health.

LET'S TALK ETHICS: A CASE STUDY APPROACH

In January, DCEG staff completed the second annual NIH training in the ethical conduct of research. The Office of Education (OE) led the charge in conducting the multi-session series, which focused on a case scenario of scientific misconduct.

Fictional Case Study

A postdoc, who had been especially prolific during his fellowship, is investigated for scientific misconduct when it's discovered that he has been using what he terms are "estimated values" for the initial manuscripts submitted to journals. He does this to expedite the review process and asserts that the final published version includes the correct data and analysis. A predoctoral fellow brings this unorthodox process to light and raises questions about the integrity of the final published results. Concerns arise about how long this has been the practice and why the mentor, a senior investigator, hasn't noted this over the past three years. The investigation was hampered because data records were not maintained.

Demetrius Albanes, M.D., Chief of the OE, serves as the DCEG representative to the NIH Committee on Scientific Conduct and Ethics. He worked on transforming the 2001 laboratory-based case to a scenario applicable in the setting of epidemiological research. Led by **Kris Kiser, M.H.A.**, the team carrying out this year's training included four DCEG facilitators: **Elizabeth McNeil, M.D.**, and **Roxana Moslehi, Ph.D., M.S.**, **Nancy Weissman, M.S.S.W.**, and **Maria Sgambati, M.D.**, and **Kit Fox,** who coordinated scheduling of the sessions and participants.

Participants grappled with questions about responsibility in scientific research, such as:

- How much verification of work should take place as researchers advance through their career?
- Who must act when doubts about the authenticity of someone's work arise?
- Is there a reluctance to challenge research supervisors?
- When should someone begin formal ethics proceedings and outside review?

Although the NIH provides clear guidelines for formal, written allegations, less guidance exists for charges in the early stages or for ambiguous situations. The case study touched on such issues as retaining data records, retracting a manuscript that contains falsified data, and divulging information about a scientist's misconduct in recommendation letters. The case-study approach enabled participants to examine how individual perspectives and career pressures change over time.

Several survey respondents noted that there were no hard-and-fast conclusions on what steps to take as events evolved. They found it easy to conclude, in hindsight, that some characters made critical mistakes in the case. However, extending from the more troubling aspects (or the uncertainties) of the case to the DCEG research environment was integral to the exercise. Current ethical and research guidelines help define some parameters, but are susceptible to human fallibility and thus interpreted with varying degrees of success.

Overall, participants favored the case-study format as a way to stimulate and focus discussion about complex ethical issues arising in a biomedical research setting. The ethics case-study is an annual requirement for all NIH staff, established in accordance with the Public Health Service Policy on the "Instruction in the Responsible Conduct of Research." The 2002 ethics training, scheduled for December, will focus on authorship issues. ■

—Kris Kiser, M.H.A.

WHAT DID THE PARTICIPANTS SAY?

Statistics

11	training sessions
154	researchers and administrators took the class
126	completed survey

Survey Responses

Was the training session useful?

Yes	120 (95%)
Somewhat useful	4 (3%)
No	2 (2%)

What did you like about it?

Overall, participants thought it was a good case study and appreciated the "lively case discussions" and "interactions among participants from different levels and with diverse points of view." Attendees also found the guidance materials on misconduct and record retention helpful.

DCEG TOWN MEETING WELCOMES NCI DIRECTOR ANDREW VON ESCHENBACH

At the annual DCEG Town Meeting on April 30, Andrew von Eschenbach, M.D., addressed the Division for the first time since assuming leadership of the NCI in January 2002. His opening remarks reflected on his 'First 100 Days' in office, which presented a major challenge after spending the past 26 years in academic medicine as a surgical oncologist at the M.D. Anderson Cancer Center in Texas. Part of his challenge has been understanding and appreciating the internal dimension of the NCI, a process that requires an enormous amount of time listening, learning, and absorbing information.

The Town Meeting's awards ceremony gave the Director an inside glimpse of DCEG and he noted that even though the Division is part of the NCI intramural program, it is "anything but intramural in the sense of your outreach to the world." Dr. von Eschenbach commended DCEG as an "incredible example of the paradigm of collaboration," which he believes is critical in advancing our knowledge of cancer and in solving the complex problems of this disease.

Dr. von Eschenbach's goal is twofold. First, he hopes to bring the NCI together with other public and private partners in concerted efforts to better understand cancer and formulate new strategies for prevention and treatment. Secondly, he plans to ensure that the Institute remains in a core leadership position. Although he understands that the "NCI can't do it all," he believes NCI holds a key position to "make sure it all gets done." Dr. von Eschenbach also described his proposed NCI management strategy.

Division members raised many questions including some related to molecular epidemiology and biospecimen repositories, new privacy regulations and their effect on DCEG research, the status of Fellows, and areas of special promise in cancer research. By attending the Town Meeting, Dr. von Eschenbach commented that he learned more about the tangible contributions DCEG makes towards research, as well as the 'intangible' contributions—the network of people behind the work.

CFC Achieves Success

Combined Federal Campaign (CFC) coordinator, **Elyse Wiszneauckas**, of the Office of the Director (OD) was recognized for her outstanding work in this year's campaign. The CFC team included branch key workers **Joseph Coble, Sc.D.**, **Jennifer Connor**, **Sandra Coopersmith**, **Kit Fox**, **Sadie Holmes**, **Andre Jimenez**, **Judy Lindley**, **Sandy Rothschild**, **Tawanda Roy**, and **Julie Russell**. This team helped DCEG achieve 149 percent of its contribution goal and a 95 percent participation rate. For its exemplary contribution, the DCEG received the CFC Campaign Presidential Award for the fourth year in a row.

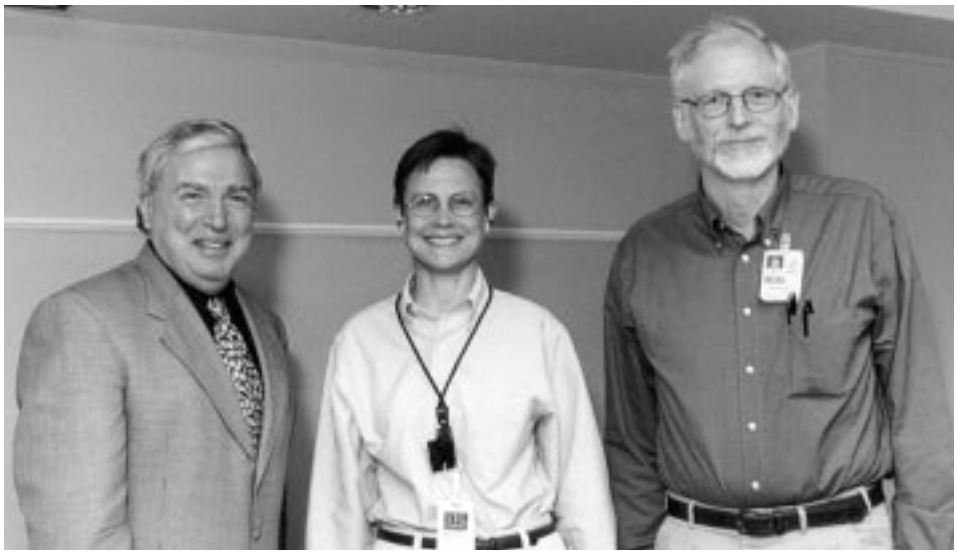
NIH Charles Harkin Award

Charles Land, Ph.D. and **Alice Sigurdson, Ph.D.** of the Radiation Epidemiology Branch (REB), along with Jeffery Struewing, M.D. (Center for Cancer Research), won the NIH Charles Harkin Award for research on thyroid cancer. The award will support their work on genetic susceptibility to thyroid cancer following nuclear fallout.

CFC Awards: Drs. Andrew von Eschenbach and Joseph F. Fraumeni, Jr. with Ms. Sandra Coopersmith, Ms. Elyse Wiszneauckas, Ms. Jennifer Connor, Ms. Catherine Fox, Ms. Julie Russell, Ms. Judith Lindley, Ms. Sandra Rothschild, and Dr. Joseph Coble

NIH Plain Language Awards

Several investigators in the DCEG were recognized for receiving NIH Plain Language awards. **Ruth Kleinerman, M.P.H.** (REB), **Margaret A. Tucker, M.D.** of the Genetic Epidemiology Branch (GEB), and Kathy Chimes (Westat) won an Award of Excellence for their brochure, *An Update from the Retinoblastoma Study*. Honorable Mentions went to **Louise Brinton, Ph.D.** of the Environmental Epidemiology Branch (EEB) and Nancy Nelson, M.S. (NCI Press Office) for their news series on research into the health effects of silicone breast implants. Nancy Nelson also won an Honorable Mention for the Fact Sheet on "NCI Research On Causes of Cancers in Children" and her press materials on the study of cell phone use and brain tumors, which was led by **Peter Inskip, Sc.D.** (REB).



NIH Charles Harkin Award: Dr. Andrew von Eschenbach with Drs. Alice Sigurdson and Charles Land

Outstanding Research Paper by a Fellow in 2001

Two outstanding papers were recognized by the DCEG Senior Advisory Group (SAG). **Anand Chokkalingam, Ph.D.** (EEB) received an award for his work entitled "Vitamin D receptor gene polymorphisms, insulin-like growth factors, and prostate cancer risk: A population-based case-control study in China," which was published in *Cancer Research*. **Rachael Stolzenberg-Solomon, M.P.H., Ph.D.** of the Nutritional Epidemiology Branch (NEB) was recognized for her paper on "*Helicobacter pylori* seropositivity as a risk factor for pancreatic cancer," published in the *Journal of the National Cancer Institute*.

Awards for Outstanding Research Paper by a Fellow in 2001: Drs. Anand Chokkalingam and Rachael Stolzenberg-Solomon with Dr. Joseph F. Fraumeni, Jr.

Outstanding Research Paper by a Staff Scientist in 2001

Linda Morris Brown, Dr.P.H. of the Biostatistics Branch (BB) was recognized for her paper entitled "Excess incidence of squamous cell esophageal cancer among U.S. Black men: Role of social class and other risk factors" published in the *American Journal of Epidemiology*.

DCEG Intramural Research Awards

These awards encourage tenure-track investigators and fellows to develop innovative and interdisciplinary research projects that bridge organizational boundaries. The four winners this year were **Lee Moore, Ph.D.** of the Occupational Epidemiology Branch (OEB) for her proposal on "VHL inactivation and its relationship with risk factors for renal cell carcinoma;" **Ulrike Peters, Ph.D.** (NEB) for her work titled "Selenium, genetic polymorphisms of selenoproteins, and prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial;" and **Rose Yang, Ph.D.** (GEB) for her proposal, "Microarrays and hormonal pathways in breast cancer." **Mingdong Zhang, M.D., Ph.D.** of the Viral

NIH Plain Language Awards: Dr. Andrew von Eschenbach with Dr. Louise Brinton, Ms. Ruth Kleinerman, and Dr. Margaret A. Tucker

Intramural Research Awards: Drs. Ulrike Peters, Lee Moore, and Abhijit Dasgupta

Epidemiology Branch (VEB) and **Abhijit Dasgupta, Ph.D.** (BB) shared an award for their proposal, "Analysis of gene expression in HCV-infected livers: Identification of genes associated with responsiveness to therapy."

Fellowship Achievement Awards

The achievement awards recognize outstanding Cancer Research Training Award fellows. The fellows are nominated by their Branch Chiefs and evaluated on the basis of scientific productivity, as demonstrated by high-quality scientific publications and ongoing research projects. In addition to a plaque, the fellows receive a two-step increase in their stipend. The 2002 awards went to REB fellows **Alina Brenner, M.D., Ph.D.**, **Deirdre Hill, Ph.D.**, and **Cecile Ronckers, Ph.D.**, as well as BB fellow **Sowmya Rao, Ph.D.**

DCEG Fellows Appreciation Award

This year, the DCEG fellows petitioned Dr. Fraumeni for a special award to be given to a member of the Division who has greatly enhanced their fellowship experience at NCI. **Kris Kiser, M.H.A.** of the Office of Education (OE), received the award for her cheerful, tireless service to DCEG Fellows in the areas of recruitment, orientation, training, and quality of work life.

DCEG Outstanding Mentoring Award

Based on votes from DCEG fellows, two outstanding mentors were selected this year: **Thomas O'Brien, M.D., M.P.H.** (VEB), and **Barry Graubard, Ph.D.** (BB). Fellows describe Dr. O'Brien as an "outstanding mentor who helped fellows set clear, achievable, short- and long-term goals; facilitated research collaborations and training; and encouraged increasing independence of fellows." The fellows commented that Dr. Graubard "patiently teaches fellows, helps them develop innovative new approaches to problems, and provides excellent career advice. He expertly guides fellows through projects, always being available yet encouraging them to grow in scientific independence."

DCEG Award for Exemplary Service

The award for exemplary service honors a DCEG scientist who combines sustained research accomplishments with outstanding service to the Division and NCI. This year's recipient was **Aaron Blair, Ph.D.** (OEB), an internationally recognized expert in occupational cancer epidemiology. Dr. Blair has made major contributions to understanding the carcinogenic effects of pesticides and industrial chemicals, as well as providing international service and leadership in environmental epidemiology. He was particularly recognized for his exemplary leadership as chief of OEB. In science and in service, Aaron Blair has been a model of excellence, innovation, and integrity to all of DCEG.

Outstanding Mentoring Awards: Dr. Andrew von Eschenbach with Drs. Thomas O'Brien and Barry Graubard

A second surprise award at the end of the meeting honored Deputy Director **Shelia Hoar Zahm, Sc.D.**, for her sustained research accomplishments and outstanding service to the Division and NCI. Dr. Zahm has assumed an incredible number and variety of responsibilities since her appointment as Deputy Director in 1998. Yet despite the heavy burden of science administration, she continues to conduct high-impact research in the area of environmental epidemiology. ■

—Maria Sgambati, M.D.

MEET THE COMMISSIONED CORPS ENSEMBLE

The Public Health Services Commissioned Corps Ensemble, formed in late 2000, performs at various events. PHS Commissioned Officers are located in various agencies within the Department of Health and Human Services (DHHS)—including NIH, Centers for Disease Control and Prevention, Food and Drug Administration, Health Resources and Services Administration—or detailed to certain agencies outside DHHS, such as the U.S. Coast Guard or EPA. Although the largest core of performers in the Ensemble comes from the Washington, DC, area, officers in any geographic region are eligible to participate.

The Ensemble consists of a choral group, a brass quintet, and an instrumental chamber group composed of stringed instruments. The choral group practices monthly and performs 8–10 times a year under the co-direction of **LCDR Mary L. McMaster, M.D.**, of the Genetic Epidemiology Branch, and LCDR Moira G. McGuire, of the Substance Abuse and Mental Health Services Administration. Dr. McMaster studied voice for 15 years, beginning in high school, and performed with the UNC Opera Theater as an undergraduate. In 1982, during her second year of medical school, she was a finalist at the state level of the Metropolitan Opera auditions. She now sings a wide variety of parts, from mezzo-soprano to alto and even tenor, if needed.

The Ensemble has led enthusiastic audiences in singing the National Anthem and the PHS March at events such as the annual meeting of the PHS Commissioned Officers Association and the annual Anchor and Caduceus luncheon. The Ensemble has also performed at several award ceremonies and, in February, they performed at Surgeon General David Satcher's retirement reception. The group has provided seasonal music for the Surgeon General's holiday reception, and they are preparing a program for the NIH Children's Inn. The Ensemble welcomes new members and performance opportunities.


Dr. MaryLou McMaster

—Mary Fraser, R.N., M.A.

RECENT SCIENTIFIC HIGHLIGHTS

GENETICS

Beckwith-Wiedemann Syndrome

The most common constitutional abnormalities in Beckwith-Wiedemann syndrome (BWS) involve abnormal DNA methylation of either *H19* or *LIT1*, genes that encode untranslated RNAs on 11p15. In a case-cohort study using data on 92 patients from the BWS Registry, the relationship between epigenetic alterations and BWS phenotypes was explored. Individuals with cancer had significantly higher frequency of *H19* alterations, compared with individuals without cancer (56 versus 17 percent, $p = 0.002$), and cancer was not associated with *LIT1* alterations. Altered DNA methylation of *LIT1* was significantly higher in patients with midline abdominal-wall defects, compared with patients without defects (65 versus 34 percent, $p = 0.012$) and in patients with macrosomia, compared with patients without macrosomia (60 versus 18 percent, $p = 0.02$). Paternal uniparental disomy of 11p15 was associated with hemihypertrophy ($p = 0.003$), cancer ($p = 0.03$), and hypoglycemia ($p = 0.05$). These results define an epigenotype-phenotype relationship in BWS, in which aberrant methylation of *H19* and *LIT1* and paternal uniparental disomy are strongly associated with cancer risk and specific birth defects. **(DeBaun MR, Niemitz EL, McNeil DE, Brandenburg SA, Lee MP, Feinberg AP. Epigenetic alterations of H19 and LIT1 distinguish patients with Beckwith-Wiedemann syndrome with cancer and birth defects. *Am J Hum Genet* 2002;70:604-611)**

Calcium, Vitamin D Receptor Polymorphisms and Colorectal Adenomas

To better understand the relationship between calcium, vitamin D, and vitamin D receptor polymorphisms and colorectal adenomas, 226 cases and 228 controls were evaluated in a study conducted at the National Naval Medical Center in Bethesda, MD. The risk of colorectal adenoma decreased by 26 percent (odds ratio [OR]= 0.74, CI = 0.60–0.92) for each 10-ng/ml increase of serum 25-hydroxyvitamin D. A weak inverse association was observed between each 100 mg of calcium intake and colorectal adenoma (OR = 0.97, CI = 0.93–1.01). A test of multiplicative interaction showed, however, that the inverse association of serum 25-hydroxyvitamin D with colorectal adenoma was stronger in subjects with calcium intake above the median ($p = 0.13$). The *Fok*I polymorphism in the gene encoding the vitamin D receptor was not significantly associated with colorectal adenoma and did not modify the effect of vitamin D or calcium. These findings suggest a protective effect for vitamin D on risk of developing colorectal adenoma. **(Peters U, McGlynn KA, Chatterjee N, Gunter N, Garcia-Closas M, Rothman N, Sinha R. Vitamin D, calcium, and vitamin D receptor polymorphism in colorectal adenomas. *Cancer Epidemiol Biomarkers Prev* 2001;12:1267-1274)**

Pooling DNA

In principle, quantitative assays on pooled DNA samples can determine the allele distribution at a particular locus, resulting in very efficient tests for association between a disease and given yields. Pooling DNA can also yield efficient estimates of the prevalence of genetic variants. Using a sample from the general population, the method for joint prevalence estimation can be extended to estimate allele frequencies and linkage disequilibrium. The measure of linkage disequilibrium is fundamental in population genetics and in determining the power of association studies. In addition, joint allelic prevalences can be used in case-control studies to estimate the relative risks of disease from joint exposures to the genetic variants. Pooled samples can reduce the number of assays required when individual testing is done. Tables estimating these savings are given. **(Pfeiffer RM, Rutter JL, Gail MH, Struewing J, Gastwirth JL. Efficiency of DNA pooling to estimate joint allele frequencies and measure linkage disequilibrium. *Genet Epidemiol* 2002;22:94-102)**

Risk Factors for NHL Based on t(14;18) Translocations

Non-Hodgkin's lymphoma (NHL) encompasses diverse subtypes that may have diverse risk factors. Archival biopsies were assayed for the t(14;18) translocation using PCR amplification. Exposures in 68 t(14;18)-positive and 114 t(14;18)-negative cases were compared with 1,245 controls. Pathogenic mechanisms appeared to vary according to subtype. In particular, family history of hemolymphatic cancer was associated with t(14;18)-negative NHL (odds ratio [OR]= 2.4, CI = 1.4–3.9), but not t(14;18)-positive NHL (OR = 1.3, CI = 0.5–3.3). Cigarette smoking was weakly associated with t(14;18)-positive NHL (OR = 1.7, CI = 0.9–3.3), but risk decreased as smoking increased. **(Schroeder JC, Olshan AF, Dent RB, Weinberg CR, Yount B, Cerhan JR, Lynch CF, Schuman LM, Tolbert PE, Rothman N, Cantor KP, Blair A. A case-control study of tobacco use and other non-occupational risk factors for t(14;18) subtypes of non-Hodgkin's lymphoma (United States). *Cancer Causes Control* 2002;13:375-382)**

HORMONE-RELATED CANCERS

Acromegaly Increases Risk for Multiple Cancer Types

A population-based cohort of patients hospitalized for acromegaly in either Sweden (1965–1993) or Denmark (1977–1993) was linked to tumor

registry data for up to 15–28 years of follow-up. Among 1,634 patients with acromegaly, 177 patients had a diagnosis of cancer compared with an expected number of 116.5 (standardized incidence ratio [SIR] = 1.5, confidence interval [CI] = 1.3–1.8). Increased risks were found for digestive system cancers (SIR = 2.1, CI = 1.6–2.7), notably of the small intestine (SIR = 6.0, CI = 1.2–17.4), colon (SIR = 2.6, CI = 1.6–3.8), and rectum (SIR = 2.5, CI = 1.3–4.2). Risks were also elevated for cancers of the brain (SIR = 2.7, CI = 1.2–5.0), thyroid (SIR = 3.7, CI = 1.8–10.9), kidney (SIR = 3.2, CI = 1.6–5.5), and bone (SIR = 13.8, CI = 1.7–50.0). The increased risk for several cancer sites among acromegaly patients may be associated with increased circulating levels of insulin-like growth factor-1 (IGF-1). Pituitary irradiation given to some patients may have contributed to the excess risks of brain tumors and thyroid cancer. **(Baris D, Gridley G, Ron E, Weiderpass E, Mellemkjaer L, Ekbom A, Olsen JH, Baron JA, Fraumeni JF Jr. Acromegaly and cancer risk: a cohort study in Sweden and Denmark. *Cancer Causes Control* 2002;13:395-400)**

Ovarian Cancer and Hormone Replacement Therapy

A 1979–1998 cohort of former participants in the Breast Cancer Detection Demonstration Project was studied to determine whether hormone replacement therapy using estrogen only, estrogen-progestin only, or both estrogen only and estrogen-progestin increases ovarian cancer risk. Among 44,241 postmenopausal women (mean age at start of follow-up, 56.6 years), 329 women who developed ovarian cancer during follow-up were identified. Adjusted time-dependent analyses showed that ever use of estrogen only was significantly associated with ovarian cancer (rate ratio [RR] = 1.6, CI, 1.2–2.0). Increasing duration of estrogen-only use was significantly associated with ovarian cancer: RRs for 10 to 19 years and 20 or more years were 1.8 (CI = 1.1–3.0) and 3.2 (CI = 1.7–5.7), respectively (p for trend < 0.001). A 7 percent (CI = 2–13) increase in RR per year of use was also found. We observed significantly elevated RRs with increasing duration of estrogen-only use across all strata of other ovarian cancer risk factors, including women with hysterectomy. The RRs for less than 2 years and 2 or more years of estrogen-progestin-only use were 1.6 (CI = 0.78–3.3) and 0.80 (CI = 0.35–1.8), respectively, and there was no evidence of a duration response (p for trend = 0.30). **(Lacey JV Jr, Mink PJ, Lubin JH, Sherman ME, Troisi R, Hartge P, Schatzkin A, Schairer C. Menopausal hormone replacement therapy and risk of ovarian cancer. *JAMA* 2002;288:334-341)**

Breast Cancer in Relation to Estrogen/Progesterone Receptor Status and Age

Age-specific breast cancer incidence rates from the Surveillance, Epidemiology, and End Results Program (SEER) were analyzed by joint estrogen receptor and progesterone receptor (ER/PR) status for 101,140 white female and 8,870 black female cases and by ER status in 706 white and black male cases diagnosed from 1992–1998. For both white and black women the age-specific rates for ER^- breast cancer ceased increasing after 50 years of age, but the age-specific rates of ER^+ breast cancer continued to increase after 50 years of age. For men ER^- cancers appear to increase at a slower rate than ER^+ cancers at older ages. In women, the rate of ER^+ cancers was greater among blacks than whites only until age 35 years, but the rate of ER^- cancers was greater among blacks than white rates at all ages. The paracrine growth model and an increase in the proliferation rate of ER^+ cells with age may explain the continued increase in post-menopausal ER^+ cancers. **(Tarone RE, Chu KC. The greater impact of menopause on ER^- than ER^+ breast cancer incidence: a possible explanation (United States). *Cancer Causes Control* 2002;13:7-14)**

LUNG CANCER

Lung Cancer Incidence in China Decreases After Stove Improvements

This study assessed whether lung cancer incidence decreased in rural Xuanwei County, China, following changes in the 1970's from burning smoky coal in firepits to stoves with chimneys. A retrospective cohort of 21,232 farmers born in homes with firepits was followed from 1976–1992. During their lifetime, 17,184 subjects (80.9 percent) changed permanently to stoves with chimneys. A hospital record search detected 1,384 cases of lung cancer (6.5 percent) during follow-up. After venting of stoves, risk ratios (RRs) for lung cancer were 0.59 (CI = 0.49–0.71) in men and 0.54 (CI = 0.44–0.65) in women. Risk reduction became unequivocal about 10 years after stove improvements were made. **(Lan Q, Chapman RS, Schreinemachers DM, Tian L, He X. Household stove improvement and risk of lung cancer in Xuanwei, China. *J Natl Cancer Inst* 2002;94:826-835)**

Radon-Related Lung Cancer in Rural China

A case-control study was conducted in a predominantly rural area of China where underground homes are characterized by high radon levels, poor ventilation, and low residential mobility. Mean radon concentrations were 230.4 Bq/m^3 for cases (n = 768) and 222.2 Bq/m^3 for controls (n = 1,659). Lung cancer risk increased with increasing radon level ($p < 0.001$). Linear models showed excess odds ratios at 100 Bq/m^3 were 0.19 (CI = 0.05–0.47) for all subjects and 0.31 (CI = 0.10–0.81) for subjects for whom coverage of the exposure interval was 100 percent. After adjustment for exposure uncertainties, risk estimates increased by 50 percent. The results indicate that increased lung

cancer risks are associated with indoor radon exposures and that the risks may equal or exceed extrapolations based on uranium miner data. **(Wang Z, Lubin JH, Wang L, Zhang S, Boice JD Jr, Cui H, Zhang S, Conrath S, Xia Y, Shang B, Brenner A, Lei S, Metayer C, Cao J, Chen KW, Lei S, Kleinerman RA. Residential radon and lung cancer risk in a high-exposure area of Gansu Province, China. *Am J Epidemiol* 2002;155:554-564)**

MELANOMA

Penetrance of germline *CDKN2A* mutations and geographic location

Germline mutations in the *CDKN2A* gene, which encodes two proteins (p16INK4A and p14ARF), are the most common cause of inherited susceptibility to melanoma. Using data from the Melanoma Genetics Consortium, 80 high-risk families with documented *CDKN2A* mutations were analyzed to determine penetrance of these mutations. *CDKN2A* mutation penetrance was estimated to be 0.30 (CI = 0.12 – 0.62) by age 50 years and 0.67 (CI = 0.31–0.96) by age 80 years. Penetrance was not significantly modified by gender or by whether the *CDKN2A* mutation altered the p14ARF protein. There was a statistically significant effect of residing in a location with a high population incidence rate of melanoma ($p = 0.003$). By age 80 years, penetrance was 0.58 in Europe, 0.76 in the United States, and 0.91 in Australia. **(Bishop DT, Demenais F, Goldstein AM, Bergman W, Bishop JN, Bressac-de Paillerets B, Chompret A, Ghiorzo P, Gruis N, Hansson J, Harland M, Hayward N, Holland EA, Mann GJ, Mantelli M, Nancarrow D, Platz A, Tucker MA; The Melanoma Genetics Consortium. Geographical variation in the penetrance of CDKN2A mutations for melanoma. *J Natl Cancer Inst* 2002;94:894-903)**

UVB Flux and Time Outdoors Predict Melanoma Risk

Sunlight is the major environmental risk factor for melanoma, but individual exposures have been difficult to quantify. To better measure individual sunlight exposure, lifetime residential history was coupled with levels of midrange UV radiation (UVB flux), based on extrapolations of data from an earlier NCI survey of UVB ground measurements in 30 areas of the U.S. Exposures were then estimated in a case-control study of 718 non-Hispanic white patients with invasive cutaneous melanoma from melanoma clinics in Philadelphia and San Francisco and 945 matched controls from outpatient clinics with similar catchment areas. A 10 percent increase in the average annual UVB flux was associated with a 19 percent (CI = 5–35) increase in individual odds for melanoma for men and 16 percent (CI = 2–32) increase for women. In men, a 10 percent increase in hours outdoors was associated with a 2.8 percent (CI = 1.2–4.5) increase in odds. Even among women who could develop a deep tan, a 10 percent increase in hours outdoors was associated with a 5.8 percent (CI = 1.4–10.4) increase in odds. The association between melanoma risk and average annual UVB flux was strong and consistent for men and for women. The association with total adult hours outdoors was notable for men of all skin types and women who develop a suntan. **(Fears TR, Bird CC, Guerry D 4th, Sagebiel RW, Gail MH, Elder DE, Halpern A, Holly EA, Hartge P, Tucker MA. Average midrange ultraviolet radiation flux and time outdoors predict melanoma risk. *Cancer Res* 2002;62:3992-3996)**

Mutations in the *CDK4* Oncogene in Melanoma-prone Families

Mutations in *CDK4*, an oncogene with cosegregating germline mutations, have been detected in only three kindreds worldwide. Sixteen American melanoma-prone families were examined for mutations in all coding exons of *CDK4*, and additional members of two previously reported families with the Arg24Cys germline *CDK4* mutation were screened. No new *CDK4* mutations were identified. In the two Arg24Cys families, the penetrance was estimated to be 63 percent. Overall, 12 out of 12 invasive melanoma patients, 0 out of 1 *in situ* melanoma patient, 5 out of 13 dysplastic nevi patients, 2 out of 15 unaffected family members, and 0 out of 10 spouses carried the Arg24Cys mutation. Dysplastic nevi did not strongly cosegregate with the Arg24Cys mutation. Although *CDK4* is a melanoma susceptibility gene, the phenotype observed in these families is more complex than just the *CDK4* mutation, suggesting that this gene plays a minor role in hereditary melanoma. **(Goldstein AM, Chidambaram A, Halpern A, Holly EA, Guerry ID, Sagebiel R, Elder DE, Tucker MA. Rarity of *CDK4* germline mutations in familial melanoma. *Melanoma Res* 2002;12:51-55)**

Dysplastic Nevi, DNA Repair, Sunlight Sensitivity, and Melanoma

A study of 132 cases with incident melanoma and 145 matched controls was conducted to determine whether DNA repair capacity (DRC) is associated with the risk of cutaneous malignant melanoma (CMM). No association was found between melanoma risk and DRC (adjusted odds ratio [OR] = 1.0, CI = 0.6–1.7). However, individuals with a low tanning ability and a low DRC had a higher risk for CMM (OR = 8.6, CI = 2.7–27.5) than did individuals with a higher tanning ability and a high DRC. Individuals with dysplastic nevi and a low DRC had a higher risk (OR = 6.7, CI = 2.4–18.6) than those lacking dysplastic nevi and having a high DRC. Subjects with dysplastic nevi and a high DRC had an intermediate risk. A likelihood ratio test gave statistically significant interactions between DRC and tanning response ($p = 0.001$) and between DRC and dysplastic nevus status ($p = 0.04$), which were independently associated with risk of CMM. DNA repair mechanisms appear to

modify the risk for melanoma in the presence of other strong risk factors, such as a low tanning ability and the presence of dysplastic nevi. **(Landi MT, Baccarelli A, Tarone RE, Pesatori A, Tucker MA, Hedayati M, Grossman L. DNA repair, dysplastic nevi, and sunlight sensitivity in the development of cutaneous malignant melanoma. *J Natl Cancer Inst* 2002;94:94-101)**

Natural History of Dysplastic Nevi and Melanoma in High-Risk Families

The clinical and histologic features of dysplastic nevi and melanoma in 33 families with more than 2 living members with invasive melanoma were followed prospectively for up to 25 years. A total of 844 individuals underwent clinical examinations and sequential photographs of melanocytic lesions were taken as part of the evaluations. When melanocytic lesions were removed, the histology was reviewed. Representative photographs and photomicrographs were selected and shown for six classes of lesions and three mutation groups. Genotyping for *CDKN2A* and *CDK4* was performed. Among the 33 families, 17 had mutations in *CDKN2A*, 2 had mutations in *CDK4*, and 14 had no mutations in either gene identified. All families had members with dysplastic nevi and melanoma, but the lesions did not appear to vary by mutation type. The majority of dysplastic nevi either remained stable or regressed, but in a few individuals it was possible to detect early melanomas by careful surveillance. **(Tucker MA, Fraser MC, Goldstein AM, Struewing JP, King MA, Crawford JT, Chiazze EA, Zametkin DP, Fontaine LS, Clark WH Jr. A natural history of melanomas and dysplastic nevi. *Cancer* 2002;94:3192-209)**

SECOND CANCERS

Solid Tumors after Chronic Lymphocytic Leukemia

Using data from the SEER program, second cancers among 16,367 individuals with chronic lymphocytic leukemia were analyzed. Solid tumors occurred in 1,820 persons (observed:expected ratio [O/E] = 1.20, CI = 1.15–1.26). Risks were similar for patients regardless of whether they received chemotherapy only as the first course of treatment (O/E = 1.21) or no treatment initially (O/E = 1.19). Significant excesses were found for Kaposi's sarcoma (O/E = 5.09), malignant melanoma (O/E = 3.18), laryngeal cancer (O/E = 1.72), and lung cancer (O/E = 1.66). Among men increased risks were found for brain cancer (O/E = 1.91), and among women increases were found for cancers of the stomach (O/E = 1.76) and bladder (O/E = 1.52). Risks of second cancers remained fairly constant throughout the follow-up period: 1.25 (less than one year), 1.25 (one to four years), 1.14 (five to nine years), and 1.16 (10 years or more). **(Hisada M, Biggar RJ, Greene MH, Fraumeni JF Jr, Travis LB. Solid tumors after chronic lymphocytic leukemia. *Blood* 2001;98:1979-1981)**

Lung Cancer Risk after Treatment for Hodgkin's Disease

A nested case-control study of 222 lung cancer cases and 444 controls was conducted within a multinational population-based cohort of 19,046 patients with Hodgkin's disease (HD) diagnosed

DCEG WELCOMES NEW *LINKAGE* EDITOR

DCEG is pleased to welcome **Maria Sgambati, M.D.**, who has taken over the myriad tasks involved in the production of *Linkage*.


Dr. Maria Sgambati

Dr. Sgambati joined DCEG in July 1998 as a clinical research fellow in the Genetic Epidemiology Branch. At that time she worked on several projects, including studies of familial chronic lymphocytic leukemia (CLL) with Drs. Neil Caporaso and Lynn Goldin. An initial task was helping write the first Familial CLL newsletter to update families on the latest CLL research developments. She also worked on the von Hippel-Lindau project with Dr. Gladys Glenn and co-authored a book chapter on CLL with Drs. Martha Linet and Susan Devesa.

Dr. Sgambati completed medical school at Wake Forest University/Bowman Gray School of Medicine in 1991. She took a three-year internal medicine residency at Hershey Medical Center and returned to Wake Forest in 1994 to continue subspeciality training in hematology and oncology. Because of an interest in cancer etiology, she took epidemiology courses while at Wake Forest.

During her time as a DCEG research fellow, Dr. Sgambati discovered that what she liked most about science and medicine was writing, explaining things to people, and discussing issues with patients. She subsequently made a career transition into scientific communications, and in the fall of 2000 took a position as scientific editor for the NCI Clinical Trials website. She returned to DCEG in January as editor of *Linkage*.

—Sandy Rothschild

in 1965–1994. An increased risk of lung cancer was associated with treatments that included alkylating agents without radiotherapy (relative risk [RR] = 4.2, CI = 2.1–8.8) and treatments that included radiation doses of 5 Gy or more without alkylating agents (RR = 5.9, CI = 2.7–13.5). Risk increased with both increasing number of cycles of alkylating agents (especially mechlorethamine and procarbazine) and increasing radiation dose (p for trend < 0.001). Lung cancer risk was elevated (about 4-fold) starting one to four years after treatment with alkylating agents, whereas the elevated risk after radiotherapy (about 7-fold) began five years after treatment and persisted for more than 20 years. Combined treatment with alkylating agents and radiotherapy had an additive risk. Tobacco use increased lung cancer risk more than 20-fold, and risks from smoking and treatment were multiplicative. The longer-than-usual latency period for lung cancer may be due in part to the immunologic and genomic instability associated with HD. **(Travis LB, Gospodarowicz M, Curtis RE, Clarke EA, Andersson M, Glimelius B, Joensuu T, Lynch CF, van Leeuwen FE, Holowaty E, Storm H, Glimelius I, Pukkala E, Stovall M, Fraumeni JF Jr., Boice JD, Gilbert E. Lung cancer following chemotherapy and radiotherapy for Hodgkin's disease. *J Natl Cancer Inst* 2002;94:182-192)**

VIRUSES

Merkel Cell Carcinoma and HIV Infection

Merkel cell carcinoma (MCC), a rare form of skin cancer, occurs more frequently in conditions of suppressed or disordered immunity, such as post-transplantation. Population-based AIDS and cancer registries in 11 geographic locations in the United States for the period 1978–1996 were used to link data. Six cases of MCC were found among the cohort of 309,365 AIDS patients, corresponding to a relative risk of 13.4 (CI = 4.9–29.1) when compared with the general population. These results suggest that immune suppression induced by HIV increases MCC risk. **(Engels EA, Frisch M, Goedert JJ, Biggar RJ, Miller RW. Merkel cell carcinoma and HIV infection. *Lancet* 2002;359:497-498)**

Use of Human Papillomavirus DNA Testing in Equivocal Papanicolaou Smears

To explore whether human papillomavirus (HPV) DNA may help standardize equivocal cervical cytologic interpretations, a three-country comparison using 188 Papanicolaou (Pap) tests was conducted. The Pap tests, collected in a study of 20,000 women in Portland, Oregon (1989–1990), had been interpreted independently by five U.S. cytopathologists and classified as "squamous atypia." For comparison, one British and two Scandinavian pathologists reviewed the slides. All eight reviewers' classifications of negative, equivocal, or abnormal Pap smears were compared using the kappa statistic. Cytologic interpretations were then compared with HPV DNA testing. Oncogenic HPV DNA detection was significantly associated with increasingly abnormal interpretations for each reader. The British reader tended to rate tests as more abnormal than the American pathologists, while the Scandinavians tended to rate tests as more normal. Reference to the HPV DNA standard clarified the tendency of readers to render systematically more or less severe interpretations. International research on cytopathology, particularly on the possible uses of HPV DNA testing, will require calibration of local cytologic definitions. **(Scott DR, Hagmar B, Maddox P, Hjerpe A, Dillner J, Cuzick J, Sherman ME, Stoler MH, Kurman RJ, Kiviat NB, Manos MM, Schiffman M. Use of human papillomavirus DNA testing to compare equivocal cervical cytologic interpretations in the United States, Scandinavia, and the United Kingdom. *Cancer* 2002;96:14-20)**

Age and Human Papillomavirus Viral Load May Improve Triage for Colposcopy

Data from the Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Triage Study were used to determine the sensitivity for detecting cervical intraepithelial neoplasia 3 and cancer plus the percentage of referrals for colposcopy. Information on oncogenic human papillomavirus (HPV) status was available for 2,198 women with atypical squamous cells of undetermined significance (ASCUS) and 848 women with low-grade squamous intraepithelial lesions (LSIL). For ASCUS, the overall sensitivity of HPV testing at 1.0 pg/mL was 96.1 percent (CI = 92.8–99.5) and varied minimally with age. HPV testing at this threshold would refer 31.2 percent of women aged 29 years or older for colposcopy as compared with more than 65 percent of younger women. Among women aged 29 years or older with ASCUS, referral for repeat cytopathology of ASCUS had a sensitivity of 90.9 percent (CI = 81.1–100.0) and would refer 50.1 percent. Among all ASCUS, HPV testing using a threshold of 10 pg/mL decreased sensitivity to 91.5 percent and referrals to 41.7 percent. More than 63 percent of LSIL would have been referred using any strategy, achieving 90 percent sensitivity. For women with ASCUS, HPV testing was highly sensitive for detecting cervical intraepithelial neoplasia 3 and cancer, with dramatically fewer referrals of older women. Neither a single HPV test nor repeat cytopathology provides useful triage for women with LSIL. **(Sherman ME, Schiffman M, Cox JT. Effects of age and human papilloma viral load on colposcopy triage: Data from the randomized atypical squamous cells of undetermined significance low-grade squamous intraepithelial lesion triage study (ALTS). *J Natl Cancer Inst* 2002;94:102-107)** ■

DCEG PEOPLE IN THE NEWS


Dr. Dalsu Baris

Dalsu Baris, M.D., Ph.D. (OEB), gave an invited talk at the National Institute on Deafness and Other Communication Disorders in March as part of the Partnership Program Seminar Series. This program, aimed at encouraging graduate and research training, offers opportunities to individuals from disadvantaged backgrounds to receive training at NIH. Dr. Baris spoke about her career path and ongoing research projects. Additional information about this program can be found at http://www.nidcd.nih.gov/about/diversity.


Dr. Erin M. Bell


Dr. Anneclaire De Roos

OEB postdoctoral fellows **Erin M. Bell, Ph.D.**, and **Anneclaire De Roos, Ph.D.**, were invited to participate in the annual meeting of the Society for Epidemiologic Research held in June in Palm Desert, California. In a spotlight session entitled "Reproductive Methods," Dr. Bell discussed methodological approaches for addressing major challenges researchers face when examining exposures during pregnancy. The title of her talk was "Time-dependent susceptibility and differential exposure opportunity in a study of fetal death." Dr. De Roos gave an invited presentation titled "Mechanistic considerations in the application and interpretation of susceptibility markers in epidemiologic studies" as part of a symposium on DNA Repair Pathways in Cancer Epidemiology.


Dr. Aaron Blair

Aaron Blair, Ph.D. (OEB), was invited to speak on "The role of occupational cancer research in understanding cancer biology" at the Union Internationale Contre le Cancer International Cancer Congress held in Oslo in June. Dr. Blair also spoke on "Where do occupational and environmental exposures fit in the genome era?" at the Conference on Epidemiology, Scientific Evidence, and Decision-Making for Health held in Italy in April. In May, he gave a talk at the Cancer Methods Workshop in Washington, DC, on "Occupational cancer in the 21st century: What are the greatest challenges?" The National Toxicology Program of the National Institute of Environmental Health Sciences' has also invited Dr. Blair to serve through June 2005 on the Board of Scientific Counselors Report on Carcinogens Subcommittee.


Dr. Andre Bouville

Andre Bouville, Ph.D. (REB), was selected in May to receive the Food and Drug Administration's Group Recognition Award for his role in the Potassium Iodide Guidance Working Group. Dr. Bouville was cited for his outstanding performance in producing a draft guide on how to reduce the risk of thyroid cancer as a result of radiation emergencies.


Dr. Linda Morris Brown

Linda Morris Brown, Dr.P.H., and **Susan Devesa, Ph.D.** (BB), along with DCEG Director **Joseph F. Fraumeni, Jr., M.D.**, co-authored a chapter on "Epidemiology of Esophageal Cancer" for the textbook *Cancer of the Upper Gastrointestinal Tract*, published in 2002 by the American Cancer Society.


Dr. Susan Devesa


Dr. Kenneth Cantor


Dr. Mustafa Dosemeci

Kenneth Cantor, Ph.D., and **Mustafa Dosemeci, Ph.D.** (OEB), were invited speakers at the Symposium on Nutrition, Environment, and Cancer held in Ankara, Turkey, in April. Dr. Cantor spoke on "Arsenic in drinking water and risk of cancer" and Dr. Dosemeci spoke on "Physical activity and risks of 15 cancer sites in Turkey." Dr. Cantor also presented an educational seminar to journalists entitled "Environmental and occupational cancer" in March. Dr. Dosemeci gave a seminar in March at the George Washington University Department of Environmental and Occupational Health on "Considering variability in assessing exposure for epidemiologic studies."


Dr. Mitchell Gail

Mitchell Gail, M.D., Ph.D. (BB), gave the R. W. Anderson Lecture at the University of Kentucky in Lexington in February. Dr. Gail's talk focused on comparing cohort, case-control, and family-based designs for estimating gene penetrance.


Dr. Sholom Wacholder

Three Biostatistics Branch members gave invited presentations at the Eastern North America Regional Meeting of the International Biometric Society held March 19 in Arlington, Virginia. **Dr. Gail** presented "On meta-analytic assessment of surrogate outcomes." **Sholom Wacholder, Ph.D.**, spoke on "Joint effects of genetic and environmental factors: Epidemiologic questions and design options." **Nilanjan Chatterjee, Ph.D.**, presented "A competing risk problem in kin-cohort estimation."


Dr. Nilanjan Chatterjee


Dr. Patti Gravitt

Patti Gravitt, Ph.D., a predoctoral fellow in the EEB, successfully defended her doctoral dissertation at The Johns Hopkins Bloomberg School of Public Health. Dr. Gravitt's thesis was titled "Human papillomavirus load as a cofactor for cervical neoplastic progression: Assessment of temporality and potential misclassification of viral load."


Dr. Ann Hsing

Ann Hsing, Ph.D. (EEB), gave a talk on "Racial and ethnic patterns of prostate cancer incidence: Etiologic implications" at the George Washington University Urology Grand Rounds in March. In February, Dr. Hsing spoke on "Molecular epidemiology of prostate cancer" at the Center of Genomics, Wake Forest University School of Medicine.

Ruth Kleinerman, M.P.H. (REB) gave an invited talk, "Second cancers following retinoblastoma," at an International Collaborative Retino-blastoma Research mini-symposium, which took place in March at the New York Presbyterian Hospital.

Charles Land, Ph.D. (REB), traveled to Ede, the Netherlands, in February to speak on "Uncertainty, low-dose extrapolation, and the threshold hypothesis" at the L. H. Gray Conference on Radiation.


Dr. Ihor Masnyk

Ihor Masnyk, Ph.D. (REB), gave an invited talk in March on "Nuclear energy and health issues in Ukraine: Chornobyl and its aftermath" at the Foreign Service Institute at the Department of State in Washington, DC.


Dr. Thomas O'Brien


Dr. Eric Engels

Thomas O'Brien, M.D., M.P.H. (VEB), edited the book *Chemokine Receptors and AIDS*. The textbook presents the latest research on the role of chemokines, chemokine receptors, and genetic variability in the susceptibility, prevention, and treatment of HIV-1, including information on the role of the *CCR5-Δ32* allele in HIV infection. **Eric Engels, M.D., M.P.H.** (VEB), co-authored a chapter with Dr. O'Brien on "Principles of Therapy for HIV-1 Infection."

Ulrike Peters, Ph.D. (NEB), received the American Association for Cancer Research Scholar-in-Training Award for 2002 for her work on "Urinary Mutagenicity and Colorectal Adenomas," which she presented at the annual meeting in April in San Francisco.


Dr. Elaine Ron

Elaine Ron, Ph.D. (REB), gave an invited talk in April on "Cancer risks from medical irradiation" at the 38th Annual Meeting of the National Council on Radiation Protection in Arlington, Virginia.


Dr. Nathaniel Rothman

At the American Association for Cancer Research meeting in April, **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (OEB), organized and co-chaired (with Dr. Regina Santella of Columbia University) an educational session on "Current Issues in the Study of Genetic Polymorphisms and Cancer Risk in Population-based Studies."


Dr. Mark Schiffman

Mark Schiffman, M.D., M.P.H. (EEB), was presented with the American Society of Colposcopy and Cervical Pathology's Scientific Achievement Award in March at the biennial meeting in Orlando. He shared the award with Dr. Diane Solomon, Division of Cancer Prevention, for their research assessing best management of the abnormal Papanicolaou smear. The Society has over 8,000 members and has presented this award only 12 times since its founding in 1964.


Ms. Vanessa Shaw

Vanessa Shaw (OEB), NIH Academy Fellow, presented her research at the 2002 NIH Postbaccalaureate Poster Day held in May. Her poster, "Evaluating Cancer Mortality Maps as a Tool to Screen the Association between Farming and Cancer Incidence in the Agricultural Health Study," was prepared in collaboration with her OEB preceptor, Dr. Michael Alavanja. Her research examined the relationship of crop production—a surrogate for pesticide exposure—with risk of prostate cancer.


Dr. Mark Sherman


Dr. Louise Brinton


Dr. Montserrat Garcia-Closas

An NCI Breast Cancer Faculty Award was presented to **Mark Sherman, M.D.** (EEB). The award will fund his proposal, "Testing and Development of a Novel Breast Cancer Tissue Microarray Resource in a Large Population-based Case-control Study." His collaborators include fellow EEB researchers **Louise Brinton, Ph.D.**, and **Montserrat Garcia-Closas, M.D., Dr.P.H.**, Dr. David Rimm from Yale University, and Drs. Robert Cornelison, Galen Hostetter, and Olli-P. Kallioniemi of the National Human Genome Research Institute.


Dr. Jorge Toro

Jorge Toro, M.D. (GEB), received two awards for his work on Hermansky-Pudlak syndrome. The 2002 Award for Young Investigators in Dermatology, one of two given this year by the American Academy of Dermatology, recognizes outstanding research in dermatology. Dr. Toro was given the award for his work "Mutation of a novel gene causes a unique form of Hermansky-Pudlak syndrome in central Puerto Rico," which was presented at the Annual Dermatology Meeting in New Orleans this February. In addition, the Hispanic Officers Advisory Committee of the PHS Commissioned Corps selected Dr. Toro as the 2001 recipient of the Juan Carlos Finlay Award. The award honors significant achievements in medical research on health care issues affecting Hispanics.


Dr. Margaret A. Tucker

Margaret A. Tucker, M.D. (GEB), gave an invited talk at the 93rd Annual Meeting of the American Association for Cancer Researchers in San Francisco held in April. Her presentation was entitled "Assessing risk in individuals with germline mutations of cancer susceptibility genes: Not as easy as it seems."


Dr. Jimmie Vaught

Jim Vaught, Ph.D. (OD), completed a year as President of the International Society for Biological and Environmental Repositories (ISBER). ISBER, created in 1999 by a group of biorepository scientists, serves as a forum for discussion of specimen collection, processing, and storage issues not comprehensively addressed by other scientific organizations. Dr. Vaught presided over 220 attendees at the society's third annual meeting, which was held in Boston. The program included podium and poster presentations, commercial exhibits, and special workshops covering biorepository safety, human subjects regulations, and specimen packaging and shipping. During 2002, ISBER will merge with the American Society for Investigative Pathology allowing ISBER greater flexibility to sponsor specialized workshops and educational programs.


Dr. Shelia Hoar Zahm

DCEG Deputy Director **Shelia Hoar Zahm, Sc.D.**, gave invited presentations on breast cancer and pesticides at the American Association for the Advancement of Science annual meeting held in Boston in February and at an International Breast Cancer Summit in Santa Cruz, California, in May. She also lectured at Yale University on case-control methodology in February and on occupational cancer epidemiology at George Washington University in March.

COMINGS … GOINGS


Ms. Kimberly Deas-Wooten

Kimberly Deas-Wooten, M.S., joined the Genetic Epidemiology Branch (GEB) as a Cancer Research Training Award fellow. Ms. Deas-Wooten completed her masters degree in chemistry at the University of North Carolina at Chapel Hill. Her graduate studies included work in environmental health and toxicology and focused on the metabolism and environmental disposition of several xenobiotics. She also volunteered at the Alachua County Health Department in Florida, where she assisted the county epidemiologist in conducting disease surveillance, provided information to the public about disease prevention strategies, and conducted site visits to investigate disease outbreaks at day-care centers. Ms. Deas-Wooten will be working closely with Dr. Maria Teresa Landi and Dr. Neil Caporaso on lung cancer and melanoma studies.


Dr. Lifang Hou

Lifang (Priscilla) Hou, M.D., Ph.D., joined the GEB in April as a visiting fellow. She obtained her degrees from Tsukuba University in Japan and subsequently completed a year of postdoctoral fellowship training at the Sidney Kimmel Cancer Center in San Diego, California. She will be working with Dr. Jorge Toro on the clinical, epidemiologic, genetic, and laboratory investigations of individuals affected with hereditary leiomyomatosis and renal cancer.


Ms. Sadie Hutson

Sadie Hutson, M.S., recently joined the Clinical Genetics Branch (CGB). Ms. Hutson obtained her master's degree in nursing from the University of Pennsylvania and is currently completing doctoral studies there, focusing on psychosocial issues in cancer genetics. She is experienced in the field of obstetrics-gynecology and has additional background in hematology and oncology. Ms. Hutson is the recipient of an American Cancer Society Doctoral Scholarship in Cancer Nursing and an NCI T32 Pre-Doctoral Fellowship in Psychosocial Oncology. Her primary focus at CGB will be psychosocial issues among participants in the Inherited Bone Marrow Failure Syndromes project, which is led by Dr. Blanche Alter.


Ms. Mindy Kaufman

Mindy Kaufman joined the DCEG Office of the Director in March as assistant to Dr. Joseph Fraumeni. Her experience spans 20 years at NIH, including 10 years in the Intramural Research Program of the National Institute of Mental Health, where she was secretary to the Chief, Laboratory of Neurochemistry. Most recently, Ms. Kaufman managed the office of the Clinical Investigations Branch in the Cancer Therapy Evalu-ation Program of NCI. During that time, she worked closely with Dr. Anna Meadows to help start NCI's Office of Cancer Survivorship. Ms. Kaufman brings with her a wealth of knowledge and experience in all aspects of government office management.


Dr. Hongchuan Li

Hongchuan Li, Ph.D., joined the Viral Epidemiology Branch as a research fellow. Dr. Li received a B.Sc. in medicine and a M.Sc. in clinical biochemistry from Chongqing University of Medical Sciences, People's Republic of China. In 1999, he completed a Ph.D. in virology at Kagoshima University, Japan. During the past three years, Dr. Li has been working as a postdoctoral fellow in the Department of Virology at Kagoshima University, focusing on phylogenetic analyses of human T cell lymphotropic virus (HTLV)-I/II infection in various parts of the world and PCR-based molecular typing of human leukocyte antigens in association with risks of HTLV-I and other virus-related malignancies. Dr. Li will be working with Dr. Michie Hisada and Dr. Denise Whitby on molecular and host genetic studies of retroviruses and associated cancers.


Ms. Ruth Medler

Ruth Medler recently joined the Environmental Epidemiology Branch as an office automation clerk. Ms. Medler is a student at Montgomery College.


Ms. Chitra Mohla

Chitra Mohla, M.S., joined DCEG in January as a scientific program specialist in the Office of Division Operations and Analysis. Ms. Mohla previously worked in the NCI Office of Scientific Opportunities. While in that office, she designed and developed 14 web sites for the working groups

supporting special initiatives of the NCI Director. Ms. Mohla received her bachelor and masters degrees in biology at the University of Delhi, India. She has 21 years of laboratory experience at Children's National Medical Center in the areas of clinical microbiology, virology, immunology, and molecular biology. Ms. Mohla will be working on the DCEG web site redesign, as well as other aspects of Division operations.


Dr. Pauline A. Mysliwiec

Pauline A. Mysliwiec, M.D., M.P.H., recently joined the Nutritional Epidemiology Branch (NEB). Dr. Mysliwiec is board-certified in gastroenterology and internal medicine and is currently in the Division of Cancer Prevention Fellowship program. She completed her M.P.H. at the Johns Hopkins Bloomberg School of Public Health in 2001. Dr. Mysliwiec has extensive clinical experience and has held positions with Kaiser Permanente Medical Group in California and the Indian Health Service, where she developed research interests in the prevalence of *H. pylori* infection and gastric carcinoma among southwestern Native American tribes. Her current projects include characterizing colorectal adenomas as predictors of adenoma recurrence and examining patterns of secondary cancers following colon cancer.


Dr. Jerry Puskin

Jerry Puskin, Ph.D., the Director for the Environmental Protection Agency's Center for Science and Risk Assessment in the Office of Radiation and Indoor Air, is on detail to the Radiation Epidemiology Branch for six months. He is working with Dr. Charles Land to investigate the application of epidemiologic studies to radiation risk assessment.


Dr. Tanuja Rastogi

Tanuja Rastogi, Sc.D., M.S., joined NEB in April as a postdoctoral fellow. Dr. Rastogi received a doctorate in nutritional epidemiology from the Harvard School of Public Health in June 2001. For her thesis project, she assessed risk factors for coronary heart disease among Indians by conducting a multicenter case-control study of acute myocardial infarctions in hospitals in India. Before joining NCI, Dr. Rastogi completed a nine-month assignment in the Epidemiology and Burden of Disease Unit at the World Health Organization in Geneva, where she assessed the global burden of micronutrient deficiencies (vitamin A deficiency, iron-deficiency anemia, and iodine-deficiency disorders). She will work

VEB HOSTS MEETING OF MULTICENTER HEMOPHILIA COHORT STUDY INVESTIGATORS

In March, **James Goedert, M.D.** of the Viral Epidemiology Branch (VEB) hosted a meeting of investigators participating in the Multicenter Hemophilia Cohort Study (MHCS-II), a prospective cohort study of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) in persons with hemophilia. Seventy collaborators from 35 institutions in six countries reviewed the progress of the study, which was launched last year, and charted a course for the future.

The general sessions included a guest speaker, Dr. Xin Wei Wang (Center for Cancer Research), who spoke on "cDNA microarray characterization of benign and malignant liver diseases." **Philip Rosenberg, Ph.D.** (BB) presented methods and preliminary results on the imputation of HCV infection dates from questionnaire data. He also presented case-cohort methods to assess the relationship of end-stage liver disease (ESLD) to polymorphisms in candidate genes. **Mingdong Zhang, M.D., Ph.D.** (VEB) discussed correlates of HCV clearance and the effects of HCV infection involving T-, B-, and NK-cell subsets. Dr. Goedert summarized the relationship of ESLD to HCV antibody patterns, genotype, and viral load. **Ehab Rabaa, M.D.** (VEB) presented preliminary results on alcohol consumption and signs of alcoholism in MHCS-II participants. Extramural collaborators presented a range of findings and proposals relevant to HCV, HIV, and their consequences.

The MHCS-II Steering Committee, co-chaired by **Eric Engels, M.D., M.P.H.** (VEB) revised procedures for providing expert advice to the MHCS-II Executive Committee; for reviewing concepts for Special Studies, which afford opportunities for initiatives by collaborators; and for facilitating newly formed Work Groups, which are charged with accomplishing the principal objectives of the MHCS-II.

Participants attended one or more of eight Work Groups on cancer, HIV, human genetics, HCV date imputation, HCV clearance, HCV therapy, hepatic abnormalities, and liver biopsy and histopathology. DCEG researchers who would like to participate in these groups in the future should contact Drs. Goedert, Engels, Rosenberg, **Thomas O'Brien**, **Charles Rabkin**, or **Denise Whitby**.

—James Goedert, M.D.

with Dr. Rashmi Sinha on a study to assess the feasibility of conducting cancer research in relation to diet within India. Additionally, she will be working on the dietary component of the Agricultural Health Study.


Dr. Jennifer Rusiecki

Jennifer Rusiecki, Ph.D., joined the Occupational Epidemiology Branch as a postdoctoral fellow in April. She recently received her doctoral degree in epidemiology from the Division of Environmental Health at the Yale School of Medicine, Department of Epidemiology and Public Health. For her dissertation, Dr. Rusiecki investigated the risk of breast cancer from exposure to organochlorine compounds and from endogenous estrogen exposure pathways. She will be working with Dr. Mary Ward on using geographic information systems to estimate exposures associated with cancer, and with Dr. Aaron Blair on cancer mortality among Coast Guard marine inspectors.


Mr. Geoffrey Tobias

Geoffrey Tobias joined the Biostatistics Branch, as a program assistant. A recent graduate of Virginia Tech, he holds a bachelor's degree in financial management, with a minor in business. Mr. Tobias has considerable computer skills, which he is using to develop an extensive database for the Branch.


Dr. Isela Velazquez

Isela Velazquez, M.D., recently joined CGB as a special volunteer. Dr. Velazquez received her medical degree from the University of Washington and completed training in pediatrics at Kaiser Permanente in Los Angeles. She is currently a fellow in pediatric hematology/oncology at the Children's National Medical Center. She will work with Dr. Blanche Alter on the Inherited Bone Marrow Failure Syndromes project.


Ms. Alyssa Voss

In January, **Alyssa Voss** joined the DCEG for a six-month health communications internship. After receiving her bachelor of science degree in biology and chemistry from Simmons College in Boston, Ms. Voss spent three years working in private and public organizations addressing the environmental impact on health, both as a volunteer for the AmeriCorps National Civilian Community Corps and as an organic chemist for an environmental firm in Massachusetts. She is concurrently completing her master of public health degree at the University of South Florida, concentrating on public health education. Since arriving, she has worked closely with DCEG Communications Coordinator Betsy Duane on a variety of projects, including handling press calls, triaging requests, training staff, and conducting mock interviews; and special projects such as the I-131 communications plan.


Dr. Stephanie Weinstein

DCEG welcomes back **Stephanie Weinstein, Ph.D.**, who recently joined NEB as a staff scientist. Dr. Weinstein received a Ph.D. in nutritional sciences, with a minor in epidemiology, from Cornell University in 1998. She completed her pre- and postdoctoral fellowship training in NEB, focusing on the role of one-carbon metabolism in carcinogenesis. Her study of folate status, homocysteine levels, and relevant genetic polymorphisms in relation to cervical cancer won her the NIH Fellows Award for Research Excellence in 2000. Following her fellowship, Dr. Weinstein worked at the U.S. Department of Agriculture where she applied her nutritional and epidemiological expertise to analyses focused on serologic versus dietary index correlations, dietary supplements, and the improvement of public use nutritional databases. Dr. Weinstein will work with Dr. Demetrius Albanes on nutritional, biochemical, and molecular risk factors for cancer. ■