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Linkage

NCI Collaboration with Chinese Center for Disease Control Clarifies Benzene–Cancer Relationship

Long-term exposure to relatively high levels of benzene causes a particular type of leukemia called acute myeloid leukemia or acute non-lymphocytic leukemia (ANLL). The U.S. Occupational Safety and Health Administration has set the maximum allowable amount of benzene in workroom air during a 40-hour workweek at 1 ppm, but there is ongoing debate as to whether this occupational limit may be too high, especially in persons with genetic susceptibility.

About 15 years ago, DCEG scientists **Richard Hayes, D.D.S., Ph.D., Martha Linet, M.D., Mustafa Dosemeci, Ph.D., Sholom Wacholder, Ph.D.**, and William Blot, a former DCEG member and lead investigator on the study, formed a collaboration with the Chinese CDC (then called the Chinese Academy of Preventive Medicine) to evaluate the risk of cancer from occupational benzene exposure. The project grew out of a Chinese national health

survey, which showed that benzene exposure was common in Chinese industry and that exposed workers were at excess risk for leukemia and other diseases. NCI and Chinese scientists, led by Dr. Xia Lin and Dr. Guilian Li, decided to partner to investigate the spectrum of diseases caused by benzene, to relate the amount of benzene exposure to disease risk, and to understand the mechanisms of benzene carcinogenicity in humans. The initial study included 75,000 benzene-exposed workers and 35,000 unexposed workers employed between 1972 and 1987 at more than 700 factories in 12 cities throughout China. The expanded study collected data on work history and exposure and followed up on each subject to ascertain vital status, cause of death for deceased workers, and incidence of any hematopoietic or lymphoproliferative malignancy or related disorder. Two expert hematopathologists,



DCEG Linkage

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

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Lois Travis, M.D., Sc.D., of DCEG, and Dr. Chin-Yang Li, of the Mayo Clinic, joined the team to strengthen the diagnostic validation component.

“The multidisciplinary NCI–Chinese CDC study, one of the longest and largest collaborations between Chinese and American scientists, engages NCI experts in cancer epidemiology, industrial exposure assessment, and hematopathology in a significant Chinese public health problem that also has important implications for the United States and other countries,” said Dr. Linet. To date, the findings from this collaboration have contributed to lowering the benzene occupational standard in China and have greatly affected the risk assessment process for environmental benzene exposures in the United States.

Although this study focuses on benzene exposure in the workplace, exposure can also occur outdoors and in the home. Most people are exposed to a small amount of benzene on a daily basis, mainly through breathing air that contains benzene from vehicular or industrial sources, while people employed in occupations using

or making benzene are exposed to higher levels. Exposure can also be through cigarette smoke, which is contaminated with benzene.

The assessment of benzene exposure and disease-response relationships in this cohort culminated in three key findings that were published in a landmark paper in the *Journal of the National Cancer Institute* (1997; 89:1065-71). First, there were significantly increased risks of ANLL and myelodysplastic syndromes (MDS) and of non-Hodgkin’s lymphoma (NHL) among exposed subjects. Second, the elevated risks of the combined grouping of ANLL/MDS and of NHL occurred at average exposures of less than 10 ppm. Third, the temporal pattern of development differed between ANLL/MDS and NHL associated with benzene exposure: the former was linked to more recent exposure, while the latter was linked with more distant (greater than ten years) exposure.

More recently, the NCI–China CDC team dug deeper into the role of genetics in benzene toxicity and carcinogenicity. This component, led by Dr. Rothman,



Workers at Chinese shoe factory (Photograph Credit: Qing Lan)



Benzene Study Investigators (Photograph Credit: Bu-Tian Ji)

includes a cross-sectional study of early biologic effect biomarkers in benzene-exposed workers in Shanghai and a case-control study of genetic susceptibility to benzene poisoning, with hematotoxicity as the main endpoint. The case-control study showed that variation in the enzymes that activate (CYP2E1) and detoxify (NQO1) benzene and its metabolites was associated with an increased risk of benzene poisoning (*Cancer Research* 1997; 57:2839-42). “This was the first report of genetic susceptibility for adverse health effects from exposure to benzene,” noted Dr. Rothman. A series of papers from these studies also noted the presence of hematotoxicity and chromosomal aberrations in workers exposed to less than 31 ppm benzene. The hematotoxicity study was used in a recent EPA review of the toxicological effects of benzene.

Current work in the NCI–China CDC collaboration includes a follow-up study of these industrial workers from 1988 to 1999, updating work histories and associated exposures and disease outcomes. These data will help refine estimates of benzene-related cancer risks and will incorporate an evaluation of factors that determine individual susceptibility to benzene-related hematotoxicity.

These new components have included scientific input from DCEG investigators **Dr. Qing Lan, Roel Vermeulen, Ph.D.,** and **Bu-Tian Ji, M.D., Dr.P.H.,** Dr. Graca Dores, an oncologist in NCI’s Division of Cancer Prevention, and Dr. Neal Young, from the National Heart, Lung, and Blood Institute, have also joined the research team. In a complementary effort, Dr. Rothman, along with Dr. Smith, from U.C. Berkeley, and Dr. Li of the China CDC, recently carried out a cross-sectional molecular epidemiology study of healthy workers exposed to relatively low levels of benzene to evaluate the early biologic effects of benzene exposure, including hematotoxicity, chromosomal damage, gene expression, and proteomic alterations. The team is also working with **Stephen Chanock, M.D., Meredith Yeager, Ph.D.,** and **Robert Welch, M.S.,** of NCI’s Core Genotyping Facility, to

examine the influence of polymorphisms in cytokine genes on hematotoxicity in benzene-exposed workers. In addition, Dr. Vermeulen, who leads the project’s exposure assessment component, is using proteomic tools to study benzene’s effect on levels of certain key chemokines.

“Taken together, the cancer cohort and early effect biomarker studies have strengthened the association between benzene exposure and the development of hematologic malignancies,” noted Dr. Hayes. “The comprehensive and unprecedented long-term research effort between NCI and China’s CDC has played and will continue to play a critical role in assessing the cancer risks and mechanism of action from relatively low levels of benzene exposure.” ■

—Lynn Rundhaugen, M.P.H.

The Benzene and Cancer Study Scientific Advisory Panel, which was formed in 2002, has provided invaluable input and oversight for the benzene studies. Members are Dr. Ellen Eisen, Chair (University of Massachusetts), Dr. David Christiani (Harvard School of Public Health), Dr. Larry Fine (NIH), Dr. Katharine Hammond (University of California, Berkeley), Dr. Richard Hornung (University of Cincinnati), Dr. Judith Karp (Johns Hopkins University), Dr. Noah Seixas (University of Washington), Dr. Jack Siemiatycki (Université de Montréal), Dr. Ellen V. Sigal (Friends of Cancer Research), and Dr. Maureen Johnson, Executive Secretary (NCI).

DENISE WHITBY BRINGS VIRAL LABORATORY EXPERTISE TO DCEG



Denise Whitby
at work in
her NCI laboratory
(Photograph Credit:
Samantha Nhan)

Anyone reading about the virus behind Kaposi's sarcoma (KS) will quickly come across **Denise Whitby's** name. But talk to her for a few minutes and you realize she's involved in multiple aspects of studying viral-associated cancers.

Dr. Whitby, along with a group of researchers that included Dr. Robin Weiss, who Whitby called "one of the foremost virologists in the U.K. and Europe," played a key role in showing that human herpesvirus-8 (HHV-8) causes KS, a disease most common in people with AIDS. Dr. Whitby and others did some of the most significant early studies on KS and HHV-8 (now also called KSHV, for Kaposi's sarcoma-associated herpesvirus).

Dr. Whitby, a native of England, received her Ph.D. at the Institute of Cancer Research in London and trained in Weiss' lab there. "I developed an interest in

disease associations and epidemiology," she said. "The opportunity to run a virology lab in association with an epidemiology group is what brought me to NCI."

As laboratory director of the Viral Epidemiology Section, located at NCI-Frederick, Dr. Whitby wears several hats. She oversees the core support that the lab provides for studies within DCEG. The lab performs routine serology and molecular studies of viruses known or thought to be associated with cancer.

In the few years she has been at NCI, Dr. Whitby has helped effect many changes in the lab. "When I arrived, most of the work was done using commercial kits and was very routine," she said. "Since I've been here, we've developed in-house assays that are more suited to the needs of the Viral Epidemiology Branch. Many of the assays are more complex, so the

nature of what we're doing is more cutting edge."

Also, she said, the lab has developed real-time PCR assays to quantify viral DNA or RNA in clinical samples. "We're also involved in doing gene expression arrays, both viral and human," she said. Dr. Whitby's interest in the genotyping and evolution of HHV-8 has meant that the lab now has expertise in these areas and can transfer techniques to studies of other viruses.

"We're currently developing an oncoviral chip," she said. "We're going to express oligonucleotides from all viruses associated with cancer, including both human and animal viruses. We will use this chip to screen for both known and unknown agents; there should be some binding if there is a related but as yet unknown virus."

Dr. Whitby is a principal investigator in the Epidemiology and Biostatistics Program. Her research there continues to focus on KS, particularly aspects of transmission, environmental cofactors for transmission and disease, and the evolution of KSHV.

She is also looking to expand her horizons a bit. "I'm increasingly interested in viral causes of lymphoma and in searching for new viruses that may be associated with cancer," she noted. "In the lab, we hope to continue to develop scalable assays that are suitable for epidemiologic research, depending on the needs of the studies we're presented with.... I also want to continue my own studies, with perhaps a greater emphasis on the lymphoma work and searching for new viruses associated with cancer." ■

—Nancy Volkers

DCEG FELLOWS BEGIN COLLOQUIUM SERIES

DCEG fellows organized and initiated a new series of monthly lectures beginning in spring 2004 as a means to foster interaction and communication of research among fellows in the Division. The idea for a DCEG Fellows Colloquium series grew from suggestions at the Fellows' Town Hall Meeting. "Colloquium" derives from a Latin word meaning "to talk together" and describes an informal meeting for the exchange of views. In this spirit, the series was originally conceived as a forum for fellows to present their research in a relaxed collegial atmosphere, to learn about the research being carried out by other fellows within the Division, and to facilitate opportunities for informal scientific interactions. It has since expanded to include featured presentations on statistical techniques and methods, particularly in areas that are quickly evolving, such as molecular genetics. With the support of DCEG's Office of Education (OE), the series is run by the fellows for the fellows, who set the agenda, recruit speakers, and ensure that relevant topics are discussed. Planning for the colloquia rotates among the branches, which allows not only shared responsibility but ensures

that a broad range of topics are included. It also allows fellows from all areas of DCEG to present their research.

The Colloquium series kicked off on April 19, 2004, with approximately 35 fellows in attendance. The Nutritional Epidemiology Branch (NEB) volunteered to be responsible for the first three meetings, with **Shih-Chen Chang, Ph.D.**, and **Unhee Lim, Ph.D.**, taking the lead. At the April and May meetings, fellows gathered to introduce themselves and talk about their research in DCEG. From these interactions, a Fellows' Research Network was established that lists all the projects in which fellows are involved. This directory will serve as a resource to foster collaboration among fellows across the Division. In June, the Colloquium featured presentations by **Jinbo Chen, Ph.D.**, **Mitchell Gail, M.D., Ph.D.**, and **Ruth Pfeiffer, Ph.D.**, of the Biostatistics Branch on the use of risk prediction models.

Robin Wilson, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB), organized the next series of meetings. The July Colloquium, led by

Kenneth Adams, Ph.D. (NEB), **Sonja Berndt, Pharm.D.** (OEEB), **Beth Brown, Ph.D.** (Viral Epidemiology Branch), and **Sarah Daugherty, M.P.H.** (OEEB), provided an introduction to haplotype analysis. The DCEG Haplotype Interest Group continued the discussion of genetic data analysis during the September meeting. In October, Dr. Brown spoke on "The Finer Points of Presentations Using PowerPoint."

"This has been a fantastic development, one that I believe will greatly further our concept of a 'community of fellows' and benefit them directly," remarked **Demetrius Albanes, M.D.**, Chief of DCEG's OE. "In addition to serving as a venue for information and knowledge sharing, it is providing opportunities for comradery, leadership, and creativity. The energy and time they have put into the colloquia reflect not only their enthusiasm and commitment to the scientific research but to continued learning." ■

—Laura Beane-Freeman, Ph.D.
and Deirdre Hill, Ph.D.

IRVA HERTZ-PICCIOTTO GIVES DISTINGUISHED LECTURE

Dr. Irva Hertz-Picciotto, a professor in the Department of Epidemiology and Preventive Medicine at the University of California, Davis, was recently honored as the DCEG Distinguished Lecturer in Occupational and Environmental Cancer. During her June 3rd visit, Dr. Picciotto spoke on "The case-control study, causal inference, and the assessment of validity" and presented a practical method for assessing and correcting for selection bias. Dr. Picciotto received her Ph.D. in epidemiology from the University of California, Berkeley. Her research has focused on environmental exposures, pregnancy outcomes, and epidemiologic methods. Her notable career includes service on scientific advisory boards for the State of California, the U.S. Environmental Protection Agency, and the National Institute of Environmental Health Sciences.

The Distinguished Lecture series, which began in 2002, is sponsored by DCEG's Occupational and Environmental Epidemiology Branch. More information is available at <http://dceg.cancer.gov/occu-DistinguishedLectures.html>.



Irva Hertz-Picciotto gives Distinguished Lecture in Occupational and Environmental Cancer
(Photograph Credit: Samantha Nhan)

AARON BLAIR WINS JOHN GOLDSMITH AWARD

Aaron Blair, Ph.D., of the Occupational and Environmental Epidemiology Branch (OEEB), received the 2003 John Goldsmith Award for Outstanding Contributions to Environmental Epidemiology. The award is presented by the International Society for Environmental Epidemiology (ISEE) in honor of Goldsmith, one of the organization's founders and early leaders. It recognizes environmental epidemiologists who serve as role models for excellence in research, unwavering promotion of environmental health, and integrity. Dr. Blair accepted the award at ISEE's annual meeting, held in August in New York City.

“Dr. Blair has led a productive group of researchers at NCI whose high-quality epidemiologic studies have often raised the bar in their innovative approaches to exposure assessment.”

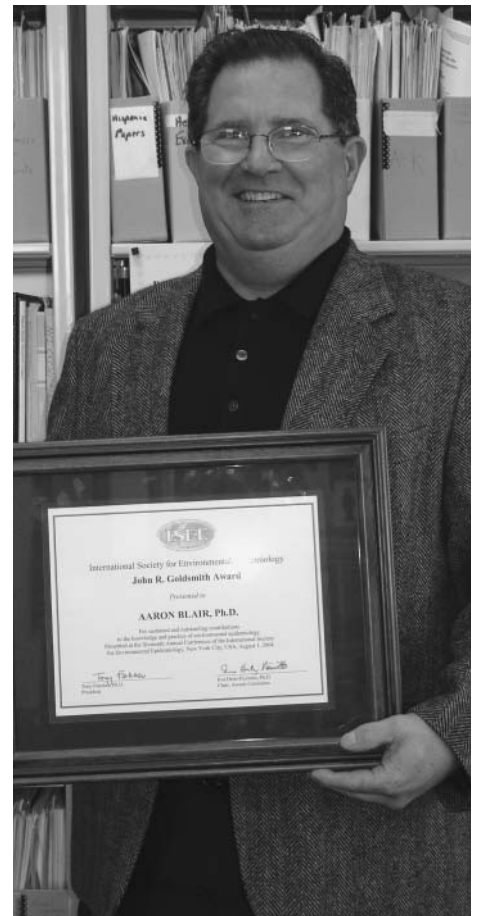
Although Dr. Blair holds a doctoral degree in evolutionary genetics, he became interested in cancer epidemiology while doing postdoctoral work in heart disease at the University of North Carolina at Chapel Hill. He arrived at NCI in 1976 and for more than 20 years has led OEEB's research program. The Branch's early research focused primarily on occupational exposures; however, under Dr. Blair's guidance, the Branch gradually expanded to incorporate environmental epidemiology. Dr. Blair's personal research includes landmark studies of industrial

workers exposed to formaldehyde, acrylonitrile, and other chemicals, as well as studies of exposure to pesticides and solvents in the workplace and in the general environment.

Dr. Blair has long championed multidisciplinary and collaborative approaches to Branch projects. In the early days of the Branch, he recruited industrial hygienists to work closely with epidemiologists on occupational studies to develop improved methods of exposure assessment, and he extended this approach to measure exposures in the general environment. Current Branch projects often incorporate sophisticated exposure assessment, biological components for mechanistic evaluation, and intensive collaboration among epidemiologists, molecular biologists, industrial hygienists, environmental engineers, and geographers.

“Dr. Blair has long been a prolific researcher in the area of environmental and occupational cancer epidemiology,” noted Dr. Irva Hertz-Picciotto, past-president of ISEE and chair of the John Goldsmith Award committee.

Dr. Blair has authored more than 200 publications on occupational and environmental causes of cancer and serves on the editorial boards for the more than a dozen journals. He is an elected board member of the American College of Epidemiology and the recipient of the NIH Director's Award, the U.S. Public Health Service Special Recognition Award, the U.S. Department of Health and Human Services Quality of Work Life Award, the DCEG Exemplary Service Award, and the University of North Carolina H.A. Tyroler Distinguished Alumni Award. He was recently elected as a fellow in the Collegium Ramazzini.



Aaron Blair wins John Goldsmith Award for Outstanding Contributions to Environmental Epidemiology
(Photograph Credit: Samantha Nhan)

In her comments at the ceremony, Dr. Hertz-Picciotto summed up the reasons for ISSE's choice of Dr. Blair: “He has led a productive group of researchers at NCI whose high-quality epidemiologic studies have often raised the bar in their innovative approaches to exposure assessment. Moreover, his exceptional mentoring of predoctoral and postdoctoral students has contributed enormously to the next generation of environmental epidemiologists. In the eyes of the International Society of Environmental Epidemiology, these accomplishments have earned Dr. Blair the John Goldsmith Award.” ■

CONFERENCE CONSIDERS RADIATION IN REALISTIC ENVIRONMENTS

In June, the American Statistical Association held its 16th conference on Radiation and Health in Beaver Creek, Colorado. **Ethel Gilbert, Ph.D.**, of the Radiation Epidemiology Branch (REB), cochaired the conference with Dr. David Brenner of Columbia University. The conference, Radiation in Realistic Environments, examined interactions between radiation and other factors, such as smoking and genetics. Approximately 60 investigators from various disciplines and workplaces attended from the United States, Canada, the United Kingdom, and Australia.

Four DCEG fellows received Young Investigator Awards to travel to and participate in the meeting: **Alina Brenner, M.D., Ph.D.** (REB), **Michael Hauptmann, Ph.D.** (BB), **Preetha Rajaraman** (REB), and **Cecile Ronckers, Ph.D.** (REB).

Invited REB speakers included **Ruth Kleinerman** who spoke on “Gene-environment interactions in irradiated retinoblastoma patients”; **Lois Travis, M.D., Sc.D.**, on “Lung cancer following Hodgkin lymphoma”; and **Alice Sigurdson, Ph.D.**, on “Second cancers after radiotherapy: Any evidence of radiation-induced genomic instability?”

The conference offered a unique forum for discussing the qualitative aspects of radiation health research in a multidisciplinary setting. Attendees had the opportunity to participate in a wide variety of discussions, for example, on whether radiation doses below one rad increase cancer risks, and the complexities in determining the risks and benefits of undergoing screening for breast and lung cancer. Many presentations focused on the carcinogenic effects of radiation exposures and the role of population variations in DNA damage and pathway



DCEG Fellows Alina Brenner, Cecile Ronckers, Preetha Rajaraman (from left) and Michael Hauptmann (sixth from left) along with other winners of the Young Investigator Award

disruption (e.g., protein-complex modification in homologous recombination or non-homologous end-joining and breast cancer). There were also presentations

about the role of *ATM* gene mutations in the sensitivity of the esophagus to radiation and to the current status of radioprotectants. ■

REB SCIENTISTS TALK ON APPLICATIONS OF RADIATION DOSIMETRY IN EPIDEMIOLOGY AT NATIONAL MEETING

On July 13, 2004, in Washington, DC, the Radiation Epidemiology Branch (REB) held a special NCI-sponsored session at the 49th annual meeting of the Health Physics Society, the world's largest society of radiation protection specialists. The session, organized by **Steve Simon, Ph.D.**, of REB, highlighted the “Uses of radiation dosimetry in epidemiologic studies.” Dr. Simon and REB Scientist **Andre Bouville, Ph.D.**, cochaired the four-hour session of 12 presentations.

The papers presented in the session are now being prepared for publication in a special issue of the journal *Radiation Research*. The first presentation, by **Martha Linet, M.D.**, Chief of REB, was an overview of the role of dosimetry in epidemiologic studies of cancer. Next was a presentation by Dr. Simon on “Dosimetric requirements for epidemiologic studies.” Other talks from REB staff were given by Dr. Bouville and **Nickolas Luckyanov, Ph.D.**, who discussed applications of dosimetry in epidemiologic studies of nuclear testing and the Chernobyl nuclear accident. **Ruth Kleinerman**, also from REB, spoke on the emerging field of retrospective assessment of exposure using biological dosimetry, and **Ethel Gilbert, Ph.D.**, discussed the statistical ramifications of dose uncertainties in radiation dose-response analyses.

The session topic, while outside the experience of most applied health physicists, was well-attended and added a new dimension to the conference. “The presentations were terrific, easy to follow, and not repetitive,” noted Dr. Linet. “I was pleased to see that this session was so well-received.”

DCEG STAFF VOLUNTEER AT CAMP FANTASTIC

About 60 miles west of NIH, near Winchester, Virginia, in the foothills of the Blue Ridge Mountains, there's a

very special camp for children with cancer. Camp Fantastic, which is run by the organization Special Love, is

a week-long, residential summer camp held every August. The camp is supported by an NCI clinical protocol, which provides medical and nursing staff for the full week.

The camp holds special meaning for the three DCEG staff members who volunteer with the program. **Stephen Chanock, M.D., Larry Chloupek, and Sheree Hawkins** all treasure the time they spend working on the Camp Fantastic program and continually find inspiration in the campers.

Dr. Chanock's NCI duties include directing the Core Genotyping Facility and serving as a senior investigator in the Pediatric Oncology Branch. He has been involved with Camp Fantastic since 1992, and in 1996 he became its medical director. He also serves on the Special Love board of directors.

Mr. Chloupek, who is Deputy Manager in DCEG's Administrative Resource



Sheree Hawkins, Stephen Chanock, and Larry Chloupek clown around for the Camp Fantastic kids

HREB LAUNCHES DISTINGUISHED LECTURER SERIES



Frank Stanczyk

The Hormonal and Reproductive Epidemiology Branch (HREB) recently established a distinguished lecturer series, which will serve as a plat-

form for outstanding scientists in the extramural community to provide input into DCEG studies on hormones and cancer. The inaugural scholar, Dr. Frank Stanczyk, Professor of Preventive Medicine at the University of Southern California, visited DCEG for three days in June. He gave a provocative seminar entitled "Measurements of steroid hormones in epidemiologic studies of breast and prostate cancers: What is missing?"

Dr. Stanczyk reviewed the formation, metabolism, and clearance of sex steroids in both men and women, and he discussed pitfalls in the measurement of steroid hormones. He pointed out that the lack of reliable immunoassays to quantify steroids in serum, urine, or tissue is a major deficiency in epidemiologic studies, and he questioned the reliability of the direct immunoassays used to quantify urinary 2-hydroxyestrone and 16 alpha-hydroxyestrone.

He challenged epidemiologists to consider measuring complete androgen/estrogen profiles and relevant metabolites in serum and tissue, particularly using gas chromatography or liquid chromatography-mass spectrometry, tools for peering into the structure of molecules by

separating them based on size and charge. He also called attention to potentially important metabolites, such as androstenedione, 5 alpha-androstenedione and DHT sulfate, which have not been measured in epidemiologic studies. Dr. Stanczyk also presented new data suggesting interactions between sex steroids and cytokines.

Dr. Stanczyk is an internationally recognized authority on the metabolism, pharmacokinetics, and measurement of steroid hormones, and he has collaborated extensively on epidemiologic studies with scientists at several cancer centers and universities as well as those at NCI.

—Ann Hsing, Ph.D.

Center (ARC), has been volunteering at Camp Fantastic since 1989. His passion is directing the camp's program for young adult cancer patients. He also serves on the board of directors and participates in numerous camp events throughout the year. Mr. Chloupek, who is also a cancer survivor, was introduced to Special Love while volunteering for the American Cancer Society. One of the society's volunteers suggested that Mr. Chloupek call the organization, believing that his skills and experiences would truly benefit Special Love. It has turned out to be a perfect match. "I really feel my experience as a cancer survivor can serve as a role model for those individuals who are going through this experience," said Mr. Chloupek. "I can provide a concrete example that one can go through this type of experience, survive, and continue to lead a productive life."

Ms. Hawkins, who is an Administrative Officer in DCEG's ARC, has been volunteering with Camp Fantastic since 1999 and helps out year-round with the massive amounts of logistical work needed to run the camp, including having all campers placed on protocol, getting outside medical staff credentialed, and transporting medications and other necessary supplies back and forth during camp week.

Started in 1983, Camp Fantastic is Special Love's hallmark program, offering a week of classes, recreation, theme parties, campfires, and other exciting activities for 7- to 17-year-old cancer patients who are currently being treated or who finished treatment within the past three years. To read more about Camp Fantastic, go to www.speciallove.org. Contributions to Special Love can be made through the combined federal campaign. ■

—Maria Sgambati, M.D.

HPV VACCINE STUDY LAUNCHES

NCI researchers, in conjunction with the Foundation for the Costa Rican Institute for Research and Training in Nutrition and Health (Fundación INCIENSA), have begun to recruit participants for a Phase III trial to evaluate whether a vaccine can protect women against infection and disease caused by two types of human papillomavirus (HPV) that are known to cause cervical cancer.

The study, which is taking place in Guanacaste, Costa Rica, is testing an HPV 16/18 virus-like particle vaccine whose technology was originally discovered at NCI and which is now being manufactured for the trial by GlaxoSmithKline Biologicals. The trial is a collaboration between NCI researchers, led by Allan Hildesheim, Ph.D., of DCEG's Hormonal and Reproductive Epidemiology Branch, and a team of over 100 researchers from the Fundación INCIENSA, headed by Dr. Rolando Herrero. Investigators hope to collect additional information on the vaccine's safety, how well it stimulates the immune system to fight HPV infection, and how effective it is at preventing the lesions that are precursors to cervical cancer.

Cervical cancer is one of the most common cancers among women worldwide. Approximately 500,000 women are diagnosed with cervical cancer each year, and more than 200,000 women die from the disease annually. Guanacaste, Costa Rica, was chosen for this study because of its high rate of cervical cancer and the many years of collaboration between NCI and the Costa Rican research team, which have resulted in an extensive knowledge of the natural history of the disease in the area.

Between 12,000 and 15,000 women, aged 18 to 25 years, will be randomized to receive the HPV 16/18 vaccine or a control vaccine. These two HPV types account for 60 to 70 percent of all cervical cancers. The vaccine is a result of decades of NCI research with Costa Rican collaborators, which causally linked HPV infection with anogenital tumors. Previous human trials in the United States led to the development of improved techniques for cervical cancer screening and to this preventive vaccine.

Study participants will receive three doses of the vaccine over a six-month period and will be followed for four years to see whether the vaccine can protect against known precursor lesions and to determine how long the vaccine protects women. Less than two months after the trial was launched, more than 800 participants had already enrolled. The NCI Principal Investigator Dr. Hildesheim comments, "I have to say that seeing a study of this magnitude launched after so many years of careful planning has been quite an experience!" ■

—Cari Kornblit



HPV Vaccine Study and Co-Principal Investigators Rolando Herrero, Ana Cecilia Rodriguez, Maria Concepcion Bratti, and Allan Hildesheim (Photograph Credit: Eric Alpizar Ocampo)

DCEG SUMMER PROGRAM CONTINUES TO ATTRACT TOP STUDENTS

DCEG once again had a highly successful summer student program. Between November and May, the Office of Education (OE) received more than 200 applications and ultimately accepted 18 students for the program. The class comprised a diverse group that represented different stages of education and included high school, undergraduate, and graduate students.

"We encourage DCEG staff at all levels to seriously consider offering rewarding summer internships to bright and enthusiastic students ... It has become clear that such early exposure to our field of research often leads to further training in epidemiology and the commitment to discovering the causes of cancer."

The 2004 program featured very gifted students, many of whom received selective grants and awards that enabled them to come to DCEG. **Jacqueline Sequoia**, a first-year Master of Public Health student at San Diego State University who worked in the Nutritional Epidemiology Branch (NEB) with **Margaret Wright, Ph.D.**, and **Demetrius Albanes, M.D.**, successfully competed for the highly selective NCI fellowship program, *Introduction to Cancer Research Careers* (ICRC), which is sponsored by the NCI's Office of Diversity and Employment Programs and Center to Reduce Cancer

Health Disparities. "I am very excited that I will be learning how to write manuscripts for publication, and I intend to use my summer research for my M.P.H. thesis," said Ms. Sequoia, in describing how she has benefited from the summer program.

Chuankai Michael Pan, a graduate of Winston Churchill High School who recently received a Robert Wood Johnson Foundation Young Epidemiology Scholar award for research he conducted during the 2003 summer program (*Linkage* July 2004), returned to DCEG this summer

to continue his analyses on smoking in relation to gallstone disease and gallbladder cancer.

The summer program would not be successful without the dedicated participation of mentors. The mentoring relationship allows students to gain knowledge by shadowing their mentors and participating in projects. "I have gained tremendous experience by taking part in the everyday activities in the world of cancer epidemiology," said **Sara Schonfeld**, a first-year graduate student

SUMMER STUDENTS AND MENTORS

BIostatistics BRANCH

- ★ **Ronald Hsu**, Harvard University. Mentor: **Philip Rosenberg, Ph.D.**
- ★ **Jiunzhu "Jane" Li**, University of Maryland and University of Michigan. Mentor: **Barry Graubard, Ph.D.**

CLINICAL GENETICS BRANCH

- ★ **Heather Bremer**, University of Maryland. Mentor: **June Peters, M.S., C.G.C.**
- ★ **Barbara Choo**, San Jose State University. Mentor: **Jennifer Loud, M.S.N., C.R.N.P.** Poster: *Ductal lavage: Tolerability in women at high genetic risk of breast cancer.*
- ★ **Kelly Yu**, Johns Hopkins School of Public Health. Mentors: **Neelam Giri, M.D.**, and **Blanche Alter, M.D.** Poster: *Clinical profile of the NCI Fanconi's anemia cohort.*

GENETIC EPIDEMIOLOGY BRANCH

- ★ **Eitan Bernstein**, Charles E. Smith Jewish Day School. Mentors: **Jorge Toro, M.D.**, and **Ousmane Toure, Ph.D.** Poster: *Inactivation of the Fumarate Hydratase Gene in tumors associated with Hereditary Leiomyomatosis Renal Cell Cancer.*
- ★ **Shannon Gnall**, University of North Carolina, Wilmington. Mentor: **Neil Caporaso, M.D.**
- ★ **Ouqi Jiang**, Massachusetts Institute of Technology. Mentors: **Jorge Toro, M.D.**, and **Ousmane Toure, Ph.D.**

NUTRITIONAL EPIDEMIOLOGY BRANCH

- ★ **Brook Calton**, Johns Hopkins School of Public Health. Mentor: **Michael Leitzmann, M.D., Dr.P.H.** Poster: *Physical activity and colon cancer risk among women: A prospective cohort study.*

from George Washington University who worked with **Lois Travis, M.D., Sc.D.**, in the Radiation Epidemiology Branch. “This experience has been incredibly helpful in learning to see the ‘big picture’ of epidemiologic research.”

Typically, more advanced scientists mentor summer students. But this year, three postdoctoral fellows—**Margaret Wright, Ph.D.** (Nutritional Epidemiology Branch), **Tanuja Rastogi, Sc.D.** (NEB), and **Sam Mbulaiteye, M.D.** (Viral Epidemiology Branch)—served as mentors. Sponsoring



DCEG summer students pictured with their mentors, along with Shelia Zahm, Joseph F. Fraumeni, Jr., and Kristin Kiser (front row, center) (Photograph Credit: Mindy Kaufman)

- ★ **Roy Kao**, Brown University. Mentor: **Tanuja Rastogi, Sc.D.** Poster: *Comparison of cancer survival among Asian Indians and Pakistanis and other races in the United States.*
- ★ **Jacqueline Sequoia**, San Diego State University School of Public Health. Mentors: **Demetrius Albanes, M.D.**, and **Margaret Wright, Ph.D.** Poster: *A prospective investigation of height and prostate cancer risk in male smokers.*

OCCUPATIONAL AND ENVIRONMENTAL EPIDEMIOLOGY BRANCH

- ★ **Tiffany Jones**, Tougaloo College. Mentors: **Lee Moore, Ph.D.**, and **Robin Wilson, Ph.D.**
- ★ **Laurie Gold**, Emory School of Public Health. Mentors: **Mary Ward, Ph.D.**, and **Roel Vermeulen, Ph.D.**
- ★ **Chuan-kai Michael Pan**, Winston Churchill High School. Mentors: **Wong Ho Chow, Ph.D.**, and **Bu-Tian Ji, M.D., Dr.P.H.**

RADIATION EPIDEMIOLOGY BRANCH

- ★ **Sara Schonfeld**, George Washington University. Mentor: **Lois Travis, M.D., Sc.D.** Poster: *Second non-germ cell solid tumors among long-term survivors of testicular cancer.*

VIRAL EPIDEMIOLOGY BRANCH

- ★ **Brandon Brown**, University of California, Irvine. Mentor: **Michie Hisada, M.D., Ph.D., Sc.D.** Poster: *Cytokine gene polymorphisms and risk of human T-lymphotropic virus type I infection in Jamaican children.*
- ★ **Laura Fraade-Blanar**, Johns Hopkins University School of Public Health. Mentor: **Eric Engels, M.D.** Poster: *AIDS-Associated Kaposi Sarcoma in Seattle, Washington and New York City: An examination of predictors based on the AIDS-Cancer Match Registry.*
- ★ **Meklit Workneh**, Stanford University. Mentor: **Sam Mbulaiteye, M.D.** Poster: *Risk for AIDS- and non-AIDS-defining cancers among persons with HIV/AIDS in Uganda: Results from the Uganda AIDS-Cancer Match Registry Study.*

a summer student is an excellent way for fellows to gain experience in mentoring and to share their growing skills. “It has been a great experience to guide a summer student,” said Dr. Mbulaiteye. “It improved my appreciation of what mentoring is all about.” He recommends that other fellows give mentoring a try but advises them to make sure they have a project the student can start right away and complete during the summer.

“We encourage DCEG staff at all levels to seriously consider offering rewarding summer internships to bright and enthusiastic students,” said Dr. Albanes, who also serves as Chief of the OE. “It’s become clear that such early exposure to our field of research often leads to further training in epidemiology and the commitment to discovering the causes of cancer.”

Kristin Kiser, M.H.A. (OE), who helped coordinate this year’s successful program, will be accepting applications for the 2005 summer beginning in November 2004. More information about the summer program can be found at the DCEG web site: <http://dceg.cancer.gov> ■

—Erin McGuigan

INTERNATIONAL WORKSHOP ON BILIARY CANCER SHOWCASES NEW FINDINGS

The Biliary Tract Cancer International Workshop, which was held in July 2004 in Shanghai, China, drew more than 150 scientists, including most of the world's experts in this field. The workshop was the culmination of a long-term collaboration between NCI and the Shanghai Cancer Institute (SCI) and showcased new results from a four-year population-based study of biliary tract cancer, the largest and most comprehensive study ever conducted on this malignancy (*Linkage*, March and September 2002).

Ann Hsing, Ph.D. (Hormonal and Reproductive Epidemiology Branch), and Dr. Yu-Tang Gao (SCI) served as cochairs. The workshop received sponsorship from NCI, SCI, the NIH Office of Rare Diseases, and the Shanghai Medical Association.

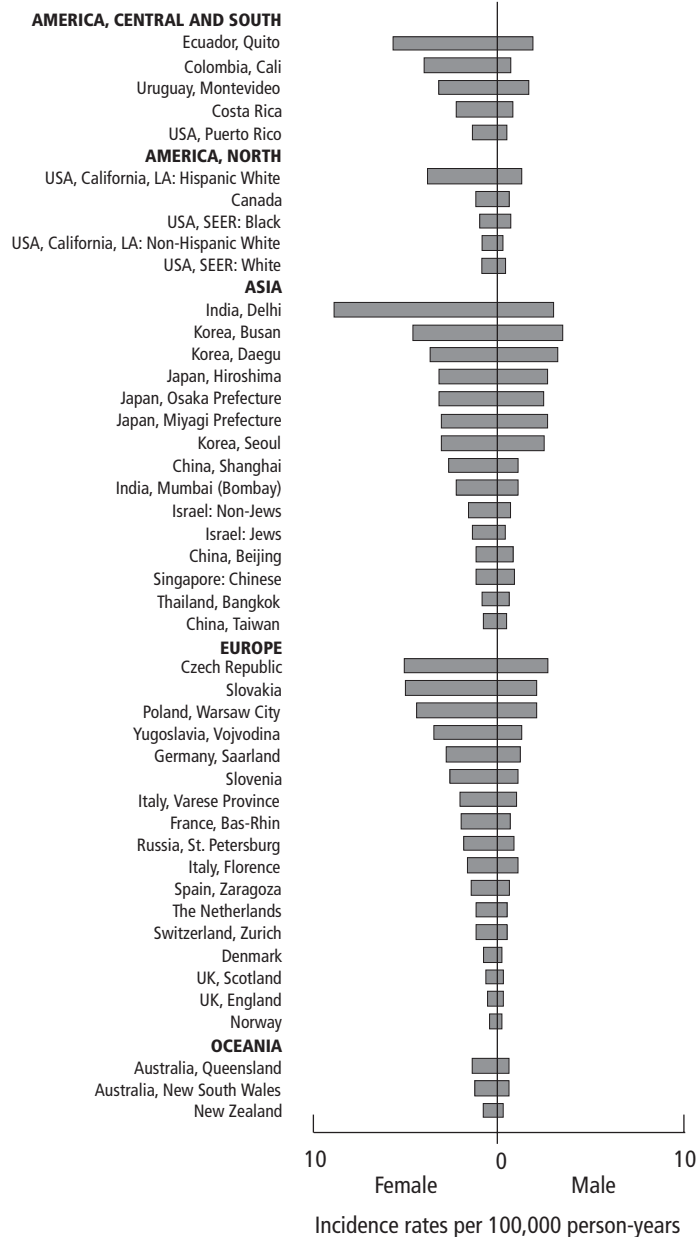
Participants included investigators from disciplines such as epidemiology, pathology, surgery, gastroenterology, genetics, and molecular biology. Held over 2 days, the workshop included presentations, panel discussions, and a poster session. Several DCEG scientists presented the results of their research, reporting positive associations of biliary tract cancer with gallstones, obesity, parity, cholecystitis, and chronic infection with hepatitis B virus, family history of gallstones, and consumption of preserved foods as well as an inverse association with use of nonsteroidal anti-inflammatory drugs. Genetic variants of apolipoprotein E, estrogen receptor, and DNA repair genes were also associated with excess risk of biliary tract cancer in China.

Dr. Albert Lowenfels of New York Medical College, the keynote speaker, gave an insightful overview of risk factors for biliary tract cancer and emphasized the need for interdisciplinary approaches to improve our understanding of the causes of this often-fatal cancer. The remainder of the two days was devoted to a wide range of topics, including demographic patterns;

risk factors; clinical management; loss of heterozygosity and other measures as tools for early diagnosis; possible role of microbial agents, including hepatitis viruses and *Helicobacter* species; identification of molecular targets for diagnosis and therapy; genetic and epigenetic factors in gallstones and biliary tract cancer; and high-throughput approaches to identifying cancer susceptibility genes. The workshop committee is planning

a meeting summary to be submitted for publication in a peer-reviewed journal. The workshop closed with a think-tank session whose participants were charged with making recommendations for future scientific research; a consensus was reached to form a consortium of investigators to forge and facilitate interdisciplinary collaboration. ■

—Ann Hsing, Ph.D.



Graph showing international variation in gallbladder cancer incidence (Hsing AW, et al. Biliary tract cancer. *Cancer Epidemiology and Prevention*. 3rd edition. New York, NY: Oxford University Press; in press)

SCIENTIFIC HIGHLIGHTS

BLADDER CANCER

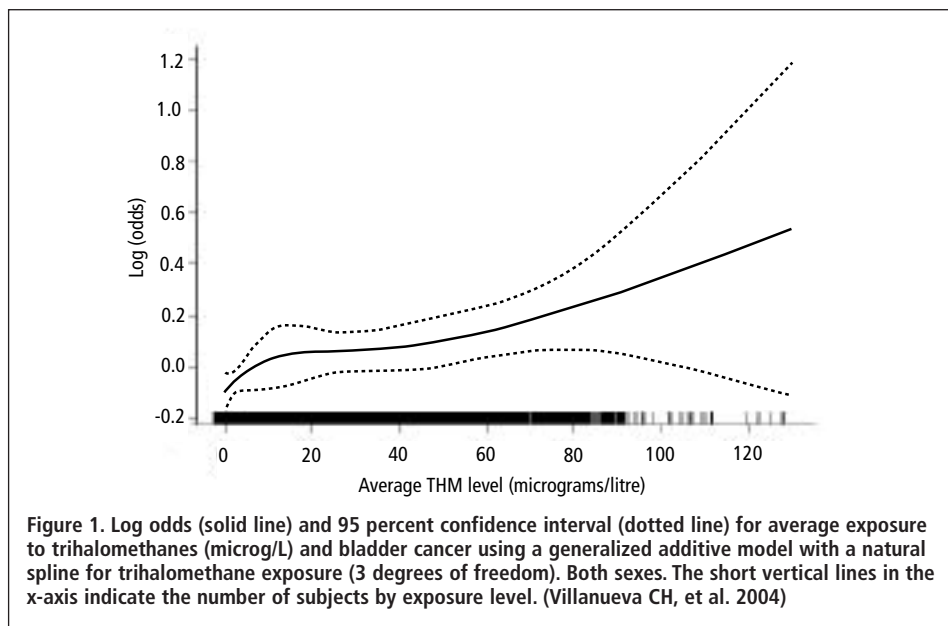
Disinfection By-products and Bladder Cancer

Disinfection by-products in drinking water may increase the risk of bladder cancer. The data from six case-control studies of bladder cancer that used trihalomethanes as a marker of disinfection by-products were pooled and analyzed (see Figure 1). Among 2,806 cases and 5,254 controls, a higher risk was seen in men exposed to an average of more than 1 microg/L (ppb) trihalomethanes than in those who had lower or no exposure (odds ratio [OR] = 1.2; confidence interval [CI] = 1.1–1.4). Estimated relative risks increased with increasing exposure and strengthen the hypothesis that the risk of bladder cancer is increased with long-term exposure to disinfection by-products at concentrations currently observed in many industrialized countries. (Villanueva CM, Cantor KP, Cordier S, Jaakkola JJ, King WD, Lynch CF, Porru S, Kogevinas M. Disinfection byproducts and bladder cancer: A pooled analysis. *Epidemiology* 2004;15:357-367)

BREAST CANCER

Breast Cancer Rates Vary by Histopathology

Age-specific incidence rate patterns for different morphologic types of breast cancer were compared using records from the SEER (Surveillance, Epidemiology, and End Results) Program registries. Age-specific incidence rate curves showed three dominant patterns: (1) rates for infiltrating duct carcinoma of no special type (duct NST), tubular, and lobular carcinomas increased rapidly until age 50 years, then rose more slowly; (2) rates for medullary and inflammatory breast carcinomas increased rapidly until age 50 years, then failed to increase; and (3) rates for papillary and mucinous carcinomas increased steadily at all ages. The patterns varied by estrogen receptor



expression and suggest that menopause has a greater impact on medullary and inflammatory carcinomas than on duct NST, tubular, and lobular carcinomas and perhaps no effect on papillary or mucinous carcinomas. (Anderson WF, Chu KC, Chang S, Sherman ME. Comparison of age-specific incidence rate patterns for different histopathologic types of breast carcinoma. *Cancer Epidemiol Biomarkers Prev* 2004;13:1128-1135)

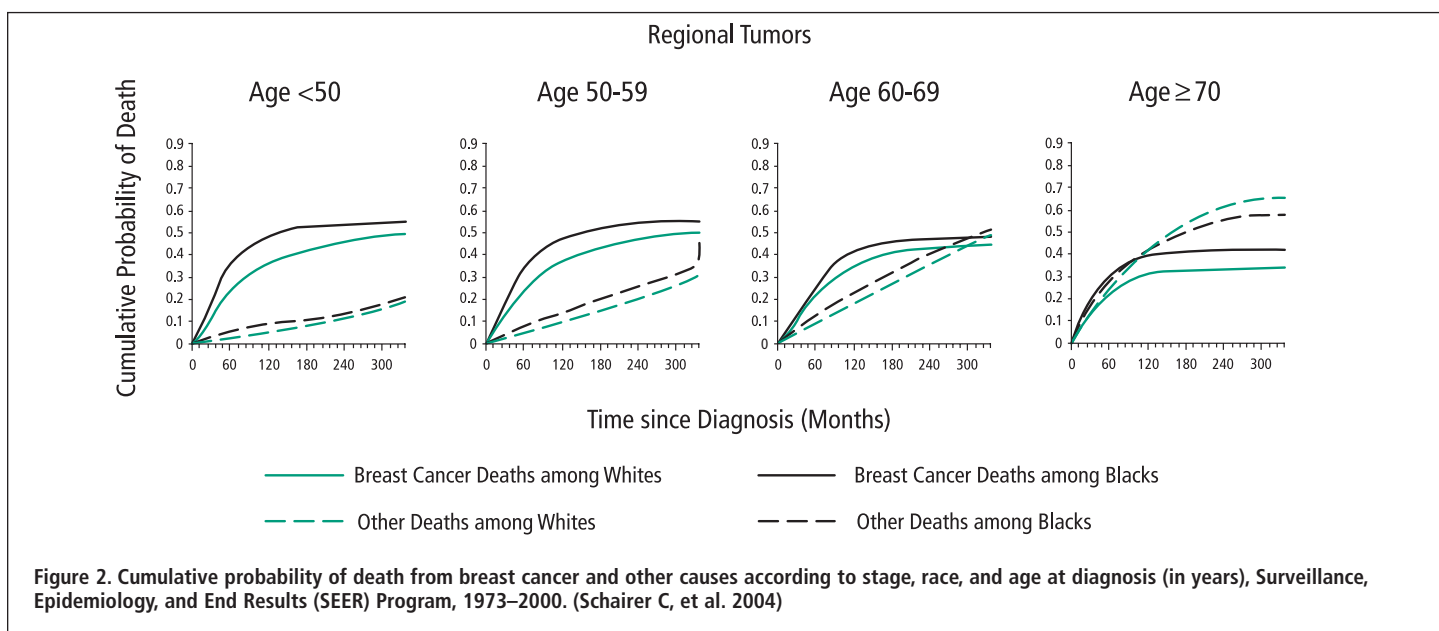
Probability of Death from Breast Cancer

Data on breast cancer patients from the Surveillance, Epidemiology, and End Results (SEER) Program were used in a competing-risk analysis to examine probabilities of death from breast cancer and other causes. Cause of death was determined for 395,251 white and 35,259 black female breast cancer patients. The probability of death (see Figure 2, page 14) from breast cancer versus other causes varied substantially depending on stage, tumor size, estrogen receptor status, and age at diagnosis in both white and black patients. (Schaier C, Mink PJ, Carroll L, Devesa SS. Probabilities of death from breast cancer and other causes among female breast cancer patients. *J Natl Cancer Inst* 2004;96:1311-1321)

CERVICAL CANCER

p16INK4a as a Prognostic Marker in Cervical HPV Infection

The use of p16INK4a immunostaining as a potential diagnostic and prognostic biomarker for cervical neoplasia was explored using paraffin-embedded tissue blocks obtained from women referred for colposcopy during the enrollment phase of the Guanacaste Project in Costa Rica. The study group included 292 women selected by HPV (human papillomavirus) status (HPV negative, nononcogenic HPV positive, or oncogenic HPV positive) and representing the diagnostic spectrum from normal to precancer, defined as cervical intraepithelial neoplasia (CIN). For CIN3, the sensitivity and specificity of diffuse p16INK4a immunostaining were 100 and 95 percent, respectively. For CIN2, the sensitivity and specificity for diffuse staining were 81.1 and 95.4 percent, respectively. Generalized to the 10,000-woman cohort, this translated to positive predictive value and negative predictive value of 13.9 percent and 100 percent, respectively, for CIN3, and 20.4 percent and 99.7 percent, respectively, for CIN2 or CIN3. Among



women with an initial diagnosis of less than CIN2, 44 percent with diffuse staining developed persistent infection at five to seven years of follow-up. (Wang SS, Trunk M, Schiffman M, Herrero R, Sherman ME, Burk RD, Hildesheim A, Bratti MC, Wright T, Rodriguez AC, Chen S, Reichert A, von Knebel Doeberitz C, Ridder R, von Knebel Doeberitz M. Validation of p16INK4a as a marker of oncogenic human papillomavirus infection in cervical biopsies from a population-based cohort in Costa Rica. *Cancer Epidemiol Biomarkers Prev* 2004;13:1355-1360)

COLORECTAL ADENOMAS

Meat Intake and the Recurrence of Colorectal Adenomas

A large randomized controlled trial was reassessed to evaluate whether reduced meat intake was associated with recurrence of adenomatous polyps of the large bowel, precursors of most colorectal malignancies. All subjects ($n = 1905$; 958 interventions and 947 controls) had one or more colorectal adenomas removed during a colonoscopy within 6 months before randomization. In the intervention group, the reduction in median meat intake was 30 percent and 31 percent for men and women, respectively, by the end of the first year. The analysis provided no evidence that lower intake or reduction in red meat consumption over four years reduces

the risk of adenoma recurrence, whereas high intake of fish was associated with lower risk of adenoma recurrence.

(Mathew A, Sinha R, Burt R, Caan B, Paskett E, Iber F, Kikendall W, Lance P, Shike M, Weissfeld J, Schatzkin A, Lanza E. Meat intake and the recurrence of colorectal adenomas. *Eur J Cancer Prev* 2004;13:159-164)

GASTRIC CANCER

Diet and Stomach Cancer Risk

A case-control study of residents diagnosed with stomach cancer during 1994 to 96 ($n = 274$) and controls ($n = 463$) from the general population was conducted in Warsaw, Poland, which has elevated rates of this cancer. Using data from direct interviews on food and beverage consumption, risk of stomach cancer was inversely related to intake of total fruits and dark green-yellow vegetables and to indices of vitamins C and E and alpha- and beta-carotenes. However, risk was not significantly increased among those with high intake of pickled/salted vegetables and sausages. Risks were positively associated with increased intake of breads/cereals/rice/pasta and other refined grains as well as a high carbohydrate index. Our findings add to the evidence of a protective effect of fruits and certain vegetables on risk of stomach cancer but do not indicate

that high intake of preserved foods like sausage has contributed to the country's elevated incidence of stomach cancer.

(Lissowska J, Gail MH, Pee D, Groves FD, Sobin LH, Nasierowska-Guttmejer A, Sygnowska E, Zatonski W, Blot WJ, Chow WH. Diet and stomach cancer risk in Warsaw, Poland. *Nutr Cancer* 2004;48:149-159)

GENETICS

Somatic *KIT* Mutations in Familial Testicular Cancer

Somatic mutations of the *KIT* gene have recently been reported in mediastinal and testicular germ cell tumors (TGCTs), particularly in cases with bilateral disease. The *KIT* coding sequence (except exon 1) was screened for germline mutations in 240 pedigrees with two or more cases of TGCT identified in an international consortium. Although no germline mutations were found, exons 10, 11, and 17 of *KIT* were examined for somatic mutations in 123 TGCT from 93 multiple-case testicular cancer families. Five somatic mutations were identified; four were missense amino-acid substitutions in exon 17 and one was a 12 bp in-frame deletion in exon 11. Two of seven TGCT from cases with bilateral disease carried *KIT* mutations, versus three out of 116 unilateral cases ($p = 0.03$). Somatic *KIT* mutations are

implicated in the development of a minority of familial as well as sporadic cases of TGCT. (Rapley EA, Hockley S, Warren W, Johnson L, Huddart R, Crockford G, Forman D, Leahy MG, Oliver DT, Tucker K, Friedlander M, Phillips KA, Hogg D, Jewett MA, Lohynska R, Daugaard G, Richard S, Heidenreich A, Geczi L, Bodrogi I, Olah E, Ormiston WJ, Daly PA, Looijenga LH, Guilford P, Aass N, Fossa SD, Heimdal K, Tjulandin SA, Liubchenko L, Stoll H, Weber W, Einhorn L, Weber BL, McMaster M, Greene MH, Bishop DT, Easton D, Stratton MR. Somatic mutations of *KIT* in familial testicular germ cell tumours. *Br J Cancer* 2004;90:2397-2401)

Risk of Head and Neck Cancer in Transplanted and Untransplanted Patients with Fanconi Anemia

Fanconi anemia (FA) patients have a high baseline risk of squamous cell cancers of the head, neck, and esophagus (SCC). Hematopoietic stem cell transplantation, the only therapy that can restore hematopoiesis in patients with FA, may increase SCC incidence. We evaluated the risks of SCC and death in 145 untransplanted FA patients in the North American Survey (NAS) cohort and 117 transplanted FA patients in the French Hopital Saint Louis (SLH) cohort. The age-specific hazard of SCC was 4.4-fold higher in transplanted than untransplanted FA patients ($p = 0.003$), and SCC occurred at significantly younger ages in the former (respective medians: 18 and 33 years, $p = 0.004$). Survival after SCC was similarly poor in both cohorts ($p = 0.135$, median = 13 months). The hazard of SCC increased at a greater than linear rate, to 4.4%/year by age 40 in NAS and 4.7%/year by 10 years after transplant in SLH. Acute and chronic graft- versus-host diseases were significant SCC risk factors. (Rosenberg PS, Socie G, Alter BP, Gluckman E. Risk of head and neck squamous cell cancer and death in transplanted and untransplanted patients with Fanconi anemia. *Blood* 2004; August 26, electronic publication before print)

Risk of Cancer in *CDKN2A* Mutation Carriers

The *CDKN2A* gene is the major known high-risk melanoma susceptibility gene and may increase risk for other cancers as well. Risk of nonmelanoma cancer was examined in 117 mutation-positive and 136 mutation-negative members from 15 families that had at least two first-degree relatives with melanoma and *CDKN2A* mutations. The families have been followed prospectively for 4 to 26 years starting in the 1970's. No significant association was seen for mutation-negative subjects (Obs/Exp = 0.3; CI = 0.0–1.2), although this group had only two observed cancers. In contrast, mutation-positive subjects had a significantly increased risk for all cancers combined (Obs/Exp = 12/5.5 = 2.2; CI = 1.1–3.8) primarily because of digestive system tumors, particularly pancreatic cancer. (Goldstein AM, Struewing JP, Fraser MC, Smith MW, Tucker MA. Prospective risk of cancer in *CDKN2A* germline mutation carriers. *J Med Genet* 2004;41:421-424)

HEMATOPOIETIC MALIGNANCIES

Familial Aggregation of Hodgkin Lymphoma

To better understand the importance of genetic factors, age, and gender on the etiology of Hodgkin lymphoma (HL), diagnoses of all lymphoproliferative malignancies were compared in 15,799 first-degree relatives of 5,047 patients with HL and 32,117 first-degree relatives of 10,078 control probands from Sweden, and in 7,185 first-degree relatives of 2,429 patients with HL and 27,434 first-degree relatives of 8,495 control probands from Denmark, using marginal survival models. An increased risk of HL in relatives of patients with HL was observed in both populations, with relative risks of 3.47 (CI = 1.77–6.80) in Sweden and 2.55 (CI = 1.01–6.45) in Denmark. In Sweden, familial risks were significantly increased for chronic lymphocytic leukemia and non-Hodgkin lymphoma.

Relative risks were higher in males than in females and in siblings than in parents and offspring of patients. Relatives of patients with earlier-onset disease were at higher risk for HL. Despite an important familial component for HL, the cumulative lifetime risks in family members are very small. (Goldin LR, Pfeiffer RM, Gridley G, Gail MH, Li X, Møller M, Olsen JH, Hemminki K, Linet MS. Familial aggregation of Hodgkin lymphoma and related tumors. *Cancer* 2004;100:1902-1908)

Occupation and Risk of Multiple Myeloma

A population-based case-control study in the U.S. was conducted to examine the relationship between occupation, living or working on a farm, pesticide exposure, and the risk of multiple myeloma (MM). Among 573 persons newly diagnosed with MM and 2,131 controls, farmers and farm workers had odds ratios (OR) of 1.9 (CI = 0.8–4.6) and 1.4 (CI = 0.8–2.3), respectively. Sheep farm residents or workers had a slightly increased risk of MM (OR = 1.7, CI = 1.0–2.7), but no increased risks were found for cattle, beef, pig, or chicken farm residents or workers. A modestly increased risk was observed for pesticide exposure (OR = 1.3; CI = 0.9–1.8). Significantly increased risks were found for pharmacists, dietitians, and therapists (OR = 6.1, CI = 1.7–22.5), service occupations (OR = 1.3; CI = 1.02–1.7), roofers (OR = 3.3; CI = 1.1–9.8), precision printing occupations (OR = 10.1; CI = 1.03–99.8), heating equipment operators (OR = 4.7; CI = 1.4–15.8), and hand molders and casters (OR = 3.0; CI = 1.0–8.4). (Baris D, Silverman DT, Brown LM, Swanson GM, Hayes RB, Schwartz AG, Liff JM, Schoenberg JB, Pottern LM, Greenberg RS, Stewart PA. Occupation, pesticide exposure and risk of multiple myeloma. *Scand J Work Environ Health* 2004;30:215-222)

INFECTIOUS AGENTS

Hepatitis C Infection and Non-Hodgkin Lymphoma

Studies have noted elevated hepatitis C virus (HCV) prevalence among patients with non-Hodgkin lymphoma (NHL), but population-based data are lacking. Population-based case-control data from a U.S. study of NHL were used to study HCV infection. Thirty-two of 813 (3.9 percent) NHL cases and 14 of 684 (2.1 percent) controls were HCV infected (OR = 2.0; CI = 1.1–4.0). Although analyses of separate NHL subtypes were based on limited numbers, positive associations were noted for follicular (OR = 2.54), marginal zone (OR = 4.0), and mucosa-associated lymphoid tissue (OR = 2.0) NHLs. Adjustment for drug use and transfusions did not affect the HCV-NHL association. These results suggest an association between HCV infection and NHL in the United States. (Engels EA, Chatterjee N, Cerhan JR, Davis S, Cozen W, Severson RK, Whitby D, Colt JS, Hartge P. Hepatitis C virus infection and non-Hodgkin lymphoma: Results of the NCI-SEER multi-center case-control study. *Int J Cancer* 2004;10:76-80)

Cancer among U.S. Army Veterans Exposed to SV40-contaminated Vaccines

Simian virus 40 (SV40) was a contaminant of vaccines produced in the 1950's and early 1960's, including a parenteral adenovirus vaccine given to several hundred thousand U.S. military recruits. A case-control study was conducted among male Army veterans to determine whether recruits receiving the SV40-contaminated adenovirus vaccine had a higher risk of cancer. Among cases of brain tumors (n = 181), mesothelioma (n = 10), and non-Hodgkin lymphoma (n = 220), the OR associated with exposure to SV40-contaminated adenovirus vaccine were 0.8 (CI = 0.5–1.2) for brain tumors, 1.4 (CI = 0.4–5.1) for mesothelioma, and 1.0 (CI = 0.6–1.4) for non-Hodgkin lymphoma. These findings do not support a role for SV40 in the development of these cancers. (Rollison DE,

Page WF, Crawford H, Gridley G, Wacholder S, Martin J, Miller R, Engels EA. Case-control study of cancer among US Army veterans exposed to simian virus 40-contaminated adenovirus vaccine. *Am J Epidemiol* 2004;160:317-324)

Maternal Poliovirus Vaccination and Risk of Childhood Cancer

To examine whether early-life simian virus 40 (SV40) infection can cause human cancer, 54,796 children enrolled in the Collaborative Perinatal Project (CPP) were studied. Among this group, 52 children had developed cancer by their eighth birthday. Children whose mothers had received pre-1963 poliovirus vaccine during pregnancy (22.5 percent) had an increased incidence of neural tumors (hazard ratio [HR] = 2.6; CI = 1.0–6.7) and hematologic malignancies (HR = 2.8; CI = 1.2–6.4). Maternal serum samples were tested for SV40 antibodies among CPP children with (n = 50) and without (n = 200) cancer. Mothers exhibited infrequent, low-level SV40 antibody reactivity, and seroconversion during pregnancy was not consistently related to children's case/control status or mothers' receipt of pre-1963 vaccine. The increased cancer risk in CPP children whose mothers received pre-1963 poliovirus vaccine was unlikely to have been due to SV40 infection transmitted from mothers to their children. (Engels EA, Chen J, Viscidi RP, Shah KV, Daniel RW, Chatterjee N, Klebanoff MA. Poliovirus vaccination during pregnancy, maternal seroconversion to simian virus 40, and risk of childhood cancer. *Am J Epidemiol* 2004;160:306-316)

LUNG CANCER

Antioxidant Intake and Risk of Lung Cancer

Higher intakes of individual antioxidants may protect against lung cancer. A dietary antioxidant index was constructed that considered multiple antioxidants simultaneously to account for potential biochemical interactions. This tool was used to predict lung cancer risk within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study cohort. Among 27,111

Finnish male smokers, 1,787 incident cases of lung cancer were identified. Principal components analyses were individually applied to the carotenoid, flavonoid, and vitamin E nutrient groups, and summation of retained principal component scores, plus selenium and vitamin C, yielded the composite antioxidant index. The relative risks for lung cancer according to increasing quintiles of the antioxidant index were 1.00 (referent), 1.00 (CI = 0.87–1.14), 0.91 (CI = 0.79–1.05), 0.79 (CI = 0.68–0.92), and 0.84 (CI = 0.72–0.98) (p for trend = 0.002). These findings support the hypothesis that a combination of dietary antioxidants reduces lung cancer risk in male smokers. (Wright ME, Mayne ST, Stolzenberg-Solomon RZ, Li Z, Pietinen P, Taylor PR, Virtamo J, Albanes D. Development of a comprehensive dietary antioxidant index and application to lung cancer risk in a cohort of male smokers. *Am J Epidemiol* 2004;1:68-76)

MALIGNANT MELANOMA

Toenail Arsenic Content and Cutaneous Melanoma

Because arsenic exposure has been linked to an increased risk of nonmelanoma skin cancer, a case-control study in Iowa examined the association of arsenic with cutaneous melanoma among subjects aged 40 years or older. Participants included 368 melanoma cases and 373 colorectal cancer controls diagnosed in 1999 or 2000. Participants completed a mailed survey and submitted toenail clippings for analysis of arsenic content by graphite furnace atomic absorption spectrophotometry. There was an increased risk of melanoma for persons with elevated toenail arsenic concentrations (OR = 2.1; CI = 1.4–3.3) and effect modification by prior skin cancer diagnosis (p for interaction = 0.03). The arsenic-melanoma findings in this study are new and thus warrant confirmation. (Beane-Freeman LE, Dennis LK, Lynch CF, Thorne PS, Just CL. Toenail arsenic content and cutaneous melanoma in Iowa. *Am J Epidemiol* 2004;160:679-687)

Diet and Risk of Melanoma

Malignant melanoma has been one of the most rapidly increasing cancers within the United States. To investigate the risk associated with dietary factors, newly diagnosed patients with melanoma ($n = 502$) were compared with controls ($n = 565$). Persons in high versus low quintiles of energy-adjusted vitamin D, alpha-carotene, beta-carotene, cryptoxanthin, lutein, and lycopene had significantly reduced risks for melanoma, which remained after adjustment for presence of dysplastic nevi, education, and skin response to repeated sun exposure.

Micronutrients from supplements did not further reduce risk. High alcohol consumption was associated with an increased risk for melanoma (OR = 1.6; CI = 1.1–2.5). Foods rich in vitamin D and carotenoids as well as limited intake of alcohol may be associated with a lower risk of melanoma. (Millen AE, Tucker MA, Hartge P, Halpern A, Elder DE, Guerry D 4th, Holly EA, Sagebiel RW, Potischman N. Diet and melanoma in a case-control study. *Cancer Epidemiol Biomarkers Prev* 2004;13:1042-1051)

Genetic Susceptibility to Melanoma

Families ($n = 55$) from the northeastern region of Italy who were prone to melanoma and had at least two relatives with melanoma were studied for genetic susceptibility markers. Multiple primary melanomas, dysplastic nevi, and pancreatic cancer were present in several families. Three known *p16* mutations—*G101W*, *R24P*, and *S56I*—and a novel *L65P* were identified in four kindreds (7 percent of all families). The *L65P* mutation caused a small distortion of *p16* tertiary structure and reduced binding to *CDK4* by 50 percent in a yeast two-hybrid assay. No disease-related mutations were found in the other tested genes (*CDKN2A*, *CDKN2B*, *p14ARF*), and there was no evidence for linkage to either chromosome 1 or 9. Germ line alterations of one or more genes other than *CDKN2A* and on chromosome loci other than those previously identified may be

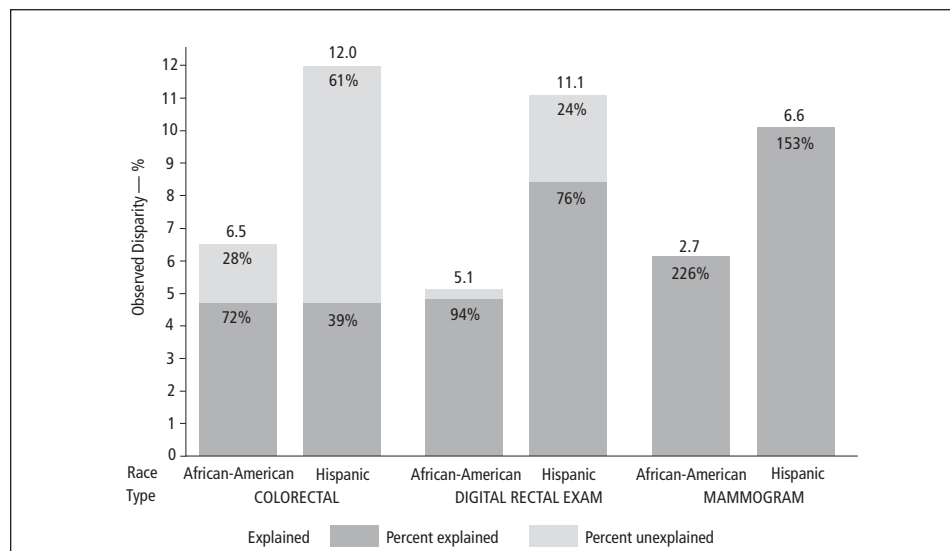


Figure 3. Percent disparity in cancer screening explained among black and Hispanic women compared to white women. The number of top of each of the bars represents the observed disparity, i.e., the difference in the crude screening rates between the non-Hispanic white women and nonwhite women (black and Hispanic). (Rao RS, et al. 2004)

important for melanoma predisposition. (Landi MT, Goldstein AM, Tsang S, Munroe D, Modi W, Ter-Minassian M, Steighner R, Dean M, Metheny N, Staats B, Agatep R, Hogg D, Calista D. Genetic susceptibility in familial melanoma from northeastern Italy. *J Med Genet* 2004;41:557-566)

METHODS

Modeling Cancer Screening Disparities

Cancer screening rates vary substantially by race and ethnicity. The Peters-Belson approach, often used in wage discrimination studies, was used to analyze disparities in cancer screening rates using the 1998 National Health Interview Survey. A regression model predicting the probability of getting screened was fitted to the majority group and was used to estimate the expected values for minority group members had they been members of the majority group. The covariates that explained the disparity in screening rates for colorectal and breast cancer between the white and the black population did not explain the disparity between the white and the Hispanic population (see Figure 3). By understanding health disparities explained by measured covariates, more effective interventions and policies can be developed. (Rao RS, Graubard BI, Breen N, Gastwirth JL. Understanding the

factors underlying disparities in cancer screening rates using the Peters-Belson approach: Results from the 1998 National Health Interview Survey. *Med Care* 2004;42:789-800)

OVARIAN CANCER

Infertility and Risk of Ovarian Cancer

To evaluate the risk of ovarian cancer as related to underlying causes of infertility, 12,193 women evaluated for infertility between 1965 and 1988 were studied. Among this cohort, 45 ovarian cancers were identified, showing a higher rate of ovarian cancer than the general female population (standardized incidence ratio [SIR] = 2.0; CI = 1.4–2.6). The risk was higher for patients with primary infertility (SIR = 2.7) than with secondary infertility (SIR = 1.4), particularly for those who never subsequently conceived (SIR = 3.3). Women with endometriosis had the highest risk (SIR = 2.5; CI = 1.3–4.2). Determination of ovarian cancer risk should take into account the type of infertility (primary versus secondary) and underlying causes. Further study of endometriosis may provide insights into ovarian carcinogenesis. (Brinton LA, Lamb EJ, Moghissi KS, Scoccia B, Althuis MD, Mabie JE, Westhoff CL. Ovarian cancer risk associated with varying causes of infertility. *Fertil Steril* 2004;82:405-414)

DCEG PEOPLE IN THE NEWS

Michael Alavanja, Dr.P.H., Occupational and Environmental Epidemiology Branch (OEEB), gave an invited talk on “Lung cancer incidence in the Agricultural Health Study” at the Toxicology Forum in Aspen, Colorado, in June. Dr. Alavanja also gave related talks at the University of Trnava, Slovakia, in July and at the International Society of Environmental Epidemiology in New York City in August.

Juan Alguacil, M.D., Ph.D. (OEEB), codirected and lectured in a course on “Use of biomarkers in epidemiological studies: Sample size, sensitivity analysis, Hardy-Weinberg equilibrium and gene-environment interactions” in Barcelona, Spain in June.

Blanche Alter, M.D., Clinical Genetics Branch (CGB), was invited to speak on “Cancer-prone rare genetic syndromes: How do they instruct us?” at the Children’s Hospital of Philadelphia in April and at the M.D. Anderson Cancer Center in Houston in September. Dr. Alter also spoke on “How do we identify individuals with Diamond-Blackfan anemia?” at the Fifth International Diamond-Blackfan Anemia Consensus Conference held during April in New York City.



Dalsu Baris

Dalsu Baris, M.D., Ph.D. (OEEB), spoke on “Epidemiology of multiple myeloma” at the International Myeloma Foundation’s Scientific Advisors Retreat in Bermuda in May. Dr. Baris also cochaired a session on evaluating molecular testing and epidemiology.

Andre Bouville, Ph.D., Radiation Epidemiology Branch (REB), organized the section on “Radiation effects” for the 11th Congress of the International Radiation Protection Association held

in Madrid, Spain, in May. The Congress was attended by about 1,200 persons from 50 countries. Other REB participants included **Elaine Ron, Ph.D.**, who chaired a plenary session on “What is known about radiation effects at low doses?”; **Martha Linet, M.D.**, who delivered a paper on the risks of hematopoietic and lymphoproliferative malignancies among U.S. radiologic technologists; and **Steven Simon, Ph.D.**, who gave a poster presentation on the estimation of the doses received by U.S. radiologic technologists.



Beth Brown

Beth Brown, Ph.D., Viral Epidemiology Branch (VEB), has been appointed as a DCEG representative to the NIH Fellows Committee. She joins

Margaret Wright, Ph.D., of the Nutritional Epidemiology Branch (NEB).



Linda Morris Brown

Capt. Linda Morris Brown, Dr.P.H., Biostatistics Branch (BB), received the Robert Brutsche Award in August at the Annual Board

Dinner of the Commissioned Officers Association (COA). This award is presented each year to a current or past

member in recognition of contributions to COA. Capt. Brown served as the Health Services category representative to the COA Board of Directors from 1998 to 2002 as a member of the Executive Committee and as Board Chair. She also chaired the Chief Professional Officer Forum at the Health Services Category Day during the PHS Professional Conference held in May in Anchorage, Alaska. Capt. Brown was deployed with the PHS-1 Disaster Medical Assistance Team during the Reagan funeral activities in June. She also gave an invited presentation on “The epidemiology of alcohol-associated cancers” at the National Institute on Alcohol Abuse and Alcoholism symposium entitled Mechanisms of Alcohol-associated Cancer, held in October in Bethesda.

Nilanjan Chatterjee, Ph.D. (BB), delivered an invited presentation, “Novel conditional-likelihoods for exploiting gene-environment independence in family-based case-control studies” in May at the International Conference on Analysis of Genomic Data in Boston and in June at the International Confer-



Nilanjan Chatterjee

ence on Statistics in the Health Sciences in Nantes, France. He also spoke on “Missing data problem in statistical genetics” in



Joanne Colt accepts her first place prize for Outstanding Poster at the American College of Epidemiology Meeting from Ahmed Arif, Texas Technology Health Sciences Center

Joanne Colt, M.P.H., M.S. (OEEB), won first place for the overall outstanding poster at the American College of Epidemiology meeting held in Boston in September. Ms. Colt’s poster was titled “Organochlorines in carpet dust and non-Hodgkin lymphoma risk.”

August at the Workshop on Missing Data Problems held at the Fields Institute for Research in Mathematical Sciences in Toronto.



Wong-Ho Chow

Wong-Ho Chow, Ph.D. (OEEB), was honored as a 2004 NCI Mentor of Merit at the annual NCI award ceremony held in October. Mentor award winners, who are nominated by their trainees, received the highest ranking in a competitive review by an advisory committee of postdoctoral fellows. The annual award recognizes NCI investigators who have proven exceptional in their commitment to fostering the independent careers of fellows, students, and other trainees.

Joseph Fraumeni, Jr., M.D., Director, DCEG, gave the keynote address on “Cancer among Native Americans: An epidemiologic perspective” at the Conference on Changing Patterns of Cancer in Native Communities in Phoenix during September.

Mark H. Greene, M.D. (CGB), gave an invited talk on “Indications for genetic testing” at the American Society for Clinical Oncology symposium on Cancer Genetics in Practice: Current Guidelines, Emerging Issues held in June in Chicago. Dr. Greene also spoke on “Prophylactic oophorectomy—surgical risk reduction in hereditary ovarian cancer” at New York University’s Lynne Cohen Foundation Symposium on the Emerging Role of Screening and Prevention in Women’s Cancer held in April in New York City.

Michael Hauptmann, Ph.D. (BB), organized and chaired a mini-symposium on Formaldehyde and Cancer during the 17th International Symposium on Epidemiology in Occupational Health in Melbourne, Australia in October.



Michael Hauptmann

Dr. Hauptmann gave a talk during the mini-symposium. He also spoke on “Cancer mortality among industrial workers exposed to formaldehyde” at the University of Washington, Seattle in April. He was a member of the Working Group for the IARC Monograph on “Formaldehyde, 2-butoxyethanol and propylene glycol mono-t-butyl ether” held in Lyon, France during June.

Richard Hayes, D.D.S., Ph.D. (OEEB), cochaired a meeting on molecular epidemiology entitled “Linking toxicology to epidemiology: Biomarkers and new technologies” in Porvoo, Finland in July.

Peter Inskip, Sc.D. (REB), received a tenure appointment in July. Dr. Inskip holds a doctoral degree in epidemiology from the Harvard School of Public Health and joined NCI as a postdoctoral fellow in 1989 before accepting a position as Associate Professor in the College of Veterinary Medicine at Texas A&M University. He returned to NCI in 1998 and launched a series of complex interdisciplinary studies in both the U.S. and abroad. With meticulous attention to study design and innovative methods, Dr. Inskip developed a research program that has provided new clues to the etiology of brain tumors, added to quantitative understanding of the risks of radiation-induced cancer, generated insights into possible carcinogenic mechanisms, and shaped the thinking and direction of research in these areas. Dr. Inskip initiated a study to address public and Congressional concerns about whether the radio-frequency radiation emitted by cellular telephones might cause brain cancer—a study which also explored a wide range of hypotheses about the etiology of these poorly understood and often fatal tumors. The study resulted in a highly publicized article in the *New England Journal of Medicine* that found no evidence of increased risk of glioma, meningioma, or vestibular schwannoma associated with use of cellular phones. Dr. Inskip was awarded an NIH Merit Award in 2001 in recognition of this work. In addition, Dr. Inskip founded and directs the Radiation Epidemiology Fellowship Program to help foster the recruitment of young investigators with expertise in the study of radiation-related cancer.

Ann Hsing, Ph.D., Hormonal and Reproductive Epidemiology Branch (HREB), served on the organizing committee for the Prostate Cancer Disparities: Science, Health Care, and Public Policy conference held in September at George Washington University. Dr. Hsing also moderated a session on demographic patterns of prostate cancer.



Jose Jeronimo

Jose Jeronimo, M.D. (HREB), received an NCI Technology Transfer Award for development of an Internet system for organizing, storing, studying, and sharing colposcopic images and for use as a research tool. The work was done in collaboration with HREB staff and with engineers from the National Library of Medicine.



Peter Inskip receives tenure

Martha Linet, M.D. (REB), gave an invited talk on “The effect of HIPAA privacy rule on research studies” at the American College of Epidemiology (ACE) meeting held in Boston in September. Dr. Linet also stepped up from president-elect to president of ACE at the meeting.

Thomas O’Brien, M.D. (HREB), chaired a spotlight session and a roundtable discussion, each on infectious disease epidemiology, at the Annual Meeting of the Society for Epidemiologic Research held in June in Salt Lake City.

Arthur Schatzkin, M.D., Dr.P.H. (NEB), spoke on “Diet and cancer: A role for molecular epidemiology?” at the United Kingdom Molecular Epidemiology Conference held in Cumbria, U.K. in September. Dr. Schatzkin also spoke on “The NIH-American Association for Retired Persons (AARP) Diet and Health Study: Physical activity and breast cancer” at the AARP national event held in Las Vegas in October. He also was invited to speak on “Surrogate end points” at the American Association for Cancer Research meeting on Frontiers in Prevention held in October in Seattle.

Mark Schiffman, M.D. (HREB), received the Food and Drug Administration’s Outstanding Service Award in June as a member of the Human Papillomavirus DNA Cervical Cytology Screening Team in recognition of his dedication to excellence in accomplishing the mission of the FDA.

Mark Sherman, M.D. (HREB), delivered the Warren Lang Lecture at the Thomas Jefferson University School of Medicine in Philadelphia in April. Dr. Sherman spoke on “Management of endometrial carcinoma precursors.”

Rashmi Sinha, Ph.D. (NEB), gave an invited talk on “Diet and cancer” at the Roche Research Chapter of Sigma Xi in October at Hoffmann-La Roche, Inc. in Nutley, New Jersey. Dr. Sinha also spoke on “Setting the bases for the creation of a database of substances formed during heat treatment” at the European Cooperation in the Field of Scientific and Technical Research meeting on Thermally Processed Foods: Possible Health Implications, held in October in Prague, Czech Republic.

Patricia Stewart, Ph.D. (OEGB), was invited to speak on “Issues for improving exposure assessment in population-based case-control studies” at the X2004 Conference in Utrecht, The Netherlands in June. At the same meeting, Dr. Stewart chaired a mini-symposium on industrial hygiene databases and chaired a session on self-reported and self-assessment of occupational exposures.

Rachael Stolzenberg-Solomon, Ph.D. (NEB), spoke on “Dietary folate intake, alcohol and post-menopausal breast cancer risk” at the Society for Epidemiologic Research meeting held in June in Salt Lake City.



Rachael Stolzenberg-Solomon

Margaret Tucker, M.D., Genetic Epidemiology Branch (GEB), spoke on “The epidemiology of melanoma: A case-control study” at the 12th Annual Meeting of the PanAmerican Society for Pigment Cell Research held in Newport Beach, California, in June 2004.

Roel Vermeulen, Ph.D. (OEGB), chaired a session on “Dermal exposure to powders” at the X2004 Conference in Utrecht, The Netherlands in June.



Roel Vermeulen

Sholom Wacholder, Ph.D. (BB), gave an invited talk on “When can we believe results of molecular epidemiology studies?” at the American College of Epidemiology meeting in Boston in September. Dr. Wacholder also served as a discussant for a symposium on sensitivity analysis at the same meeting.

Mary Ward, Ph.D. (OEGB), chaired a symposium on Drinking Water Nitrate and Health at the International Society of Environmental Epidemiology in New York City in August.

UPDATE ON RADIOLOGIC TECHNOLOGISTS STUDY

The U.S. Radiologic Technologists Study (USRT), the largest health study of medical radiation workers ever conducted, is preparing to launch a third participant survey. In preparation, study investigators, which include Radiation Epidemiology Branch members, collaborators at the University of Minnesota, and members of the American Registry of Radiologic Technologists, have published the second USRT newsletter. The newsletter presents information on recent research findings, an explanation of how radiation doses are estimated, and a question-and-answer section.



U.S. Radiologic Technologists Study web site now available at <http://www.radtechstudy.org>

The USRT study began in 1982 with the aim of quantifying the carcinogenic risks of long-term, low-dose, fractionated radiation through occupation exposures and determining applicability of current risk estimates, which are based primarily on studies of individuals experiencing single or short-term, high-dose exposures, such as atomic bomb survivors and medically irradiated patients. More than 110,000 technologists are participating in the study. The USRT has developed a new web site (<http://www.radtechstudy.org>) that includes information for study participants, researchers, and the general public.

COMINGS . . . GOINGS

Cara Frankenfeld, Ph.D., has joined the Nutritional Epidemiology Branch (NEB) as a cancer prevention fellow. Dr. Frankenfeld earned an M.S. in nutritional sciences from the University of Arizona and a Ph.D. in epidemiology from the University of Washington. During predoctoral and postdoctoral work at the Fred Hutchinson Cancer Research Center, she evaluated markers of intestinal bacteria profiles in relation to serum hormones, urinary estrogen metabolites, mammographic density, and bone mineral density in postmenopausal women. She also evaluated the familial aggregation and segregation of these phenotypes as well as *in vitro* studies on daidzein metabolism by intestinal bacteria. She is especially interested in the role played by intestinal microbiota and specific nutrients, particularly flavonoids and other phenolic compounds, in cancer risk.



Benjamin Hulley

Benjamin Hulley has joined the Genetic Epidemiology Branch (GEB) as a postbaccalaureate fellow. Mr. Hulley graduated in June from the University of California, San Diego with a double major in cell biology/biochemistry and management science (economics). During college, he worked as a research assistant on a clinical trial of statins and conducted preliminary analyses of the data. Mr. Hulley also interned at Genentech and worked as a laboratory technician in projects identifying genes contributing to susceptibility to multiple sclerosis. During his time at GEB, Mr. Hulley plans to gain experience in various aspects of conducting family- and population-based research into the determinants of cancer susceptibility.

Daehee Kang, M.D., Ph.D., an Associate Professor in epidemiology at the Seoul National University College of



Daehee Kang

Medicine, has joined the Occupational and Environmental Epidemiology Branch (OEEB) for a two-year sabbatical under the auspices of the Oak Ridge Institute for Scientific Exchange. Dr. Kang holds an M.D. from Seoul National University and a Ph.D. in environmental health sciences from Johns Hopkins University. He is an experienced molecular and environmental epidemiologist with interests in cancer risks from exposure to polycyclic aromatic hydrocarbons, solvents, and pesticides. While in the OEEB he will work on several population cohort studies.

Gregory Kirk, M.D., Ph.D., completed a postdoctoral fellowship with the Viral Epidemiology Branch (VEB) and accepted a position as Assistant Professor of Infectious Disease Epidemiology at the Johns Hopkins Bloomberg School of Public Health. Dr. Kirk first joined VEB in 1996 as a Special Volunteer. He spent most of 1997 through 1999 in Gambia, West Africa, where he launched and supervised the Gambia Liver Cancer Study of hepatocellular carcinoma. From 1999 to 2003, while continuing to monitor work in Gambia, Dr. Kirk completed a residency in internal medicine at Georgetown University, a clinical fellowship in infectious diseases at the National Institute of Allergy and Infectious Diseases, and a doctoral degree in epidemiology from Johns Hopkins University. Working with **James Goedert, M.D.**, and Dr. Ruggero Montesano, Dr. Kirk used the data and specimens from the Gambia Liver Cancer Study as the basis for his dissertation, "The epidemiology of viral, environmental and genetic factors in hepatocellular carcinoma: A case-control study from The Gambia, West Africa." Dr. Kirk served on the DCEG Technical Evaluation of Questionnaires committee

and as coordinator of VEB's hepatocellular carcinoma working group.

Cari Kornblit has joined the Office of the Director as a health communications fellow. Ms. Kornblit received her undergraduate degree in biology from New York University (NYU) in 1999 and is currently pursuing a master's degree in professional writing with a specialization in science and medical communications at Carnegie Mellon University in Pitts-



Cari Kornblit

burgh. Before venturing into writing, she worked in molecular biology research for more than six years. During that time, Ms. Kornblit received an independent research grant from Children's Hospital of Pittsburgh and worked in laboratories at NYU and, most recently, at the University of Pittsburgh, where she managed and conducted research in a molecular cardiology laboratory. She will be working with **Betsy Duane-Potocki** on various communication projects.



Ola Landgren

Ola Landgren, M.D., Ph.D., has joined GEB as a visiting fellow. A native of Stockholm, Sweden, Dr. Landgren received his medical and doctoral degrees from the Karolinska Hospital and Institute in Stockholm. For his thesis, he studied diagnostic and prognostic characteristics in Hodgkin lymphoma patients with special reference to the elderly. He is a board-certified specialist in hematology, internal medicine, and pain management and holds a consultant position at the Karolinska Hospital. Dr. Landgren will be collaborating with **Lynn Goldin, Ph.D.**, **Neil Caporaso, M.D.**, and **Mary McMaster, M.D.**, on studies related to

familial lymphoproliferative tumors and precursor conditions.



Karla Lawson

Karla Lawson, Ph.D., a cancer prevention fellow, has joined the NEB. Dr. Lawson received a Ph.D. in nutritional sciences from the University of Texas at Austin in 2003. She earned a Bachelor of Science degree in nutrition from the University of Texas at Austin in 1998, where she completed the registration exam and was certified as a registered dietitian. In 2004, she received an M.P.H. from Johns Hopkins University, concentrating in biostatistics and epidemiology. Her master's research examined the interaction between estimated calcium intake and a polymorphism in the vitamin D receptor on prostate cancer risk. Dr. Lawson's current interests include the effects of supplemental and dietary vitamin E on cancer risk and prevention.



Annette Molinaro

Annette Molinaro, Ph.D., has joined the Biostatistics Branch (BB) as a cancer prevention fellow. Dr. Molinaro received her master's and doctoral degrees in biostatistics from the University of California, Berkeley. Her dissertation involved predicting survival outcomes with high-dimensional explanatory variables. During her fellowship she will continue exploring new algorithms for building predictors with genomic and proteomic data. In addition, Dr. Molinaro will compare cross-validation techniques for model selection and assessment in small sample sizes.

Lindsay Morton, Ph.D., has joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a postdoctoral fellow. Dr. Morton recently received her doctoral degree in epidemiology from

Yale University, where her dissertation research focused on the association between hepatitis C and non-Hodgkin lymphoma (NHL). She also conducted the first pooled analysis of smoking, alcohol, and NHL risk in InterLymph, the international consortium of lymphoma case-control studies. Dr. Morton also worked in the Yale Emerging Infections Program conducting research on chronic liver disease and conducted clinical trials



Lindsay Morton

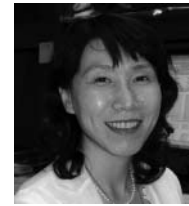
at the Massachusetts General Hospital. While at DCEG, she plans to pursue her interests in viral, genetic, and hormonal etiology of cancers.



Christine Mueller

Christine Mueller, D.O., has joined the Clinical Genetics Branch (CGB) as a clinical cancer genetics fellow. Dr. Mueller comes to NCI from the University of Pittsburgh, where she was an Assistant Clinical Professor in the Center for Medical Genetics, Department of Family Medicine. She received her degree in medicine in 1998 from the Ohio University College of Osteopathic Medicine, where she also earned board certification in family medicine. Dr. Mueller then completed a clinical medical genetics fellowship at the University of Pittsburgh School of Medicine, and she is board eligible in medical genetics. She is formally trained in dysmorphology and will be responsible for that aspect of patient care, data collection, and analysis in CGB's Inherited Bone Marrow Failure Syndromes study. She will also be developing new projects related to hereditary breast/ovarian cancer, early detection of ovarian cancer, and familial bladder cancer.

Sue Kyung Park, M.D., Ph.D., has joined the HREB as a postdoctoral fellow. Dr. Park received her medical degree from the Kyungpook National University of



Sue Kyung Park

South Korea in 1991. She completed a radiation oncology residency at the Asan Medical Center in 1994 and a preventive medicine residency at the Seoul National University in 1997. After passing specialty boards in both preventive and occupational medicine, Dr. Park received a Ph.D. from the Seoul National University in 1999, where her doctoral research involved genetic polymorphisms and breast cancer risk. She is currently an Assistant Professor of Preventive Medicine at The Konkuk University College of Medicine of South Korea. During her stay in HREB, Dr. Park plans to study the role of endogenous hormones in the development of cancers in women.



Beata Peplonska

Beata Peplonska, M.D., Ph.D., has joined OEEB as a special volunteer for one year. Dr. Peplonska is Chief of the Epidemiological Unit at the Nofer Institute of Occupational Medicine in Lodz, Poland. She has an M.D. from the Medical Academy in Lodz and a Ph.D. from the Nofer Institute. Dr. Peplonska is the field director for the Lodz component of the Breast, Ovary, and Endometrial Cancer Study in Poland led by **Louise Brinton, Ph.D.**, and **Montserrat Garcia-Closas, M.D., Dr.P.H.** She will analyze data on occupational exposures and breast cancer during her stay in DCEG.



Sowmya Rao

Sowmya Rao, Ph.D., a postdoctoral fellow in BB since 2001, has accepted a survey position with Abt Associates in Cambridge, Massachusetts. While in DCEG, she developed methods to adjust for missing data in the analysis of standardized incidence ratios and

applied these methods to an analysis of the X-Ray Technologists Study. Using the National Health Interview Survey, Dr. Rao developed and applied methods to evaluate racial/ethnic disparities in cancer screening rates. She also analyzed data collected from NIH postdoctoral fellows to evaluate NIH-wide mentoring.

Katherine Roberts, a predoctoral fellow in NEB since 2003, has left to begin her Ph.D. in chronic disease epidemiology at Johns Hopkins Bloomberg School of Public Health. While in DCEG, Ms. Roberts completed her M.P.H. and worked with **Rachael Stolzenberg-Solomon, Ph.D.**, on a literature review of studies examining weight loss and hormone changes in women. She also conducted analyses on one-carbon polymorphisms in the Navy colorectal polyps study and on characteristics of the insulin resistance syndrome and colorectal cancer.

Monica Ter-Minassian, M.S., who had been a predoctoral fellow in GEB since 2002, has left to enter the doctoral program at the Harvard School of Public Health. Ms. Ter-Minassian's ultimate goal



Monica Ter-Minassian

is to focus on genetic and molecular epidemiology in the field of cancer research. During her time in DCEG, she worked with **Lynn Goldin, Ph.D.**, and **Maria Landi, M.D., Ph.D.**, on linkage analysis within the Italian familial melanoma study.

Isabelle Thierry-Chef, Ph.D., has joined the Radiation Epidemiology Branch as a postdoctoral fellow. Dr. Thierry-Chef previously worked as a



Isabelle Thierry-Chef

research scientist at the Institute for Radiation Protection and Nuclear Safety (IRSN) in France and received her Ph.D. in environmental science from

the University of Provence, France. Her doctoral research, which was conducted at the International Agency for Research on Cancer, involved the study of errors in dosimetry within an international collaborative study of cancer risk among workers in the nuclear industry. At ISRN, Dr. Thierry-Chef conducted a feasibility study of health effects resulting from multiple x-rays among a population of premature babies. While at REB, she hopes to conduct a similar feasibility study in the U.S. and gain experience in the assessment of uncertainties associated with medical, occupational, and environmental exposures.

Robin Wilson, Ph.D., a postdoctoral fellow in OEEB since 2002, has taken a position as Assistant Professor in the Department of Health Sciences at the Hershey Medical Center, Pennsylvania State College of Medicine. During her fellowship, Dr. Wilson analyzed occupational risks of salivary gland tumors, used geographic information system

approaches in epidemiologic studies, and participated in studies of second primaries among cancer survivors.



Yawei Zhang

Yawei Zhang, M.D., Ph.D., has joined HREB as a postdoctoral fellow. Dr. Zhang received a Doctor of Medicine degree from West China University of Medical Sciences and an M.P.H. and Ph.D. (epidemiology) from Yale University. For her doctoral dissertation, Dr. Zhang investigated the association between non-Hodgkin lymphoma (NHL) and a variety of exposures, including farm and nonfarm use of pesticides, use of hair-coloring products, and ultraviolet exposure from sun and other sources. Dr. Zhang also investigated gene-environment interactions as related to risks of lymphoma, breast cancer, and multiple myeloma. While at DCEG, she plans to pursue her interests in testicular cancer and NHL.

DCEG EXPANDS INTRAMURAL RESEARCH AWARD PROGRAM

In order to provide more competitive funding opportunities for fellows and tenure-track scientists, DCEG has expanded its Intramural Research Award (IRA) program to two yearly funding cycles: one in the spring and one in the fall. Each cycle will fund up to three proposals.

The IRA program recognizes small, innovative, interdisciplinary research projects being led by tenure-track investigators and fellows in the Division. These projects often cross usual organizational boundaries. Individuals are eligible to receive up to \$75,000 a year in research funds, and the award is renewable for up to three years. Each proposal is reviewed by a member of the NCI Board of Scientific Counselors or another extramural scientist with appropriate expertise and by senior DCEG scientists. The proposals are judged on potential for significant scientific or public health impact, innovative aspects of the approach or methodology, interdisciplinary and collaborative nature of the project, ability to achieve the objectives within the proposed time frame and with the proposed resources, and programmatic relevance to the Division. The award can be combined with funds from other sources to support a larger project.

DAVID PAWEL RECEIVES BEEBE FELLOWSHIP

Dr. David Pawel, a statistician in the Radiation Protection Division of the Environmental Protection Agency (EPA), recently completed the Beebe Fellowship. The fellowship honors **Gilbert Wheeler Beebe, Ph.D.** (1912–2003), a renowned radiation epidemiologist who conducted groundbreaking studies of mortality and morbidity among persons exposed to the atomic bombings in Japan and to the Chernobyl reactor accident in Ukraine and who spent the last 25 years of his career working at NCI. During the fellowship, scientists spend time working at the Radiation Epidemiology Branch (REB) and the Radiation Effects Research Foundation (RERF) in Hiroshima, Japan, on research related to the atomic bomb survivors and other radiation topics.

Dr. Pawel, who holds a doctoral degree in statistics from the University of Wyoming, had spent a few early years in his career (1992–1994) working at the RERF. “The Beebe Fellowship not only allowed me to work at RERF again, but provided another opportunity to take

advantage of the relationship between our center and REB,” said Dr. Pawel.

During his first tour at the RERF, he worked with two prominent cytogeneticists, Dr. Akio Awa and Dr. Nori Nakamura, and others on using frequency of stable chromosome aberrations to validate the reconstructed radiation dose estimates that underlie estimates of dose-related cancer risk. Their study showed a lower dose response for stable chromosome aberrations among Nagasaki factory workers than other atomic bomb survivors, suggesting that doses for the factory workers may have been substantially overestimated. The finding contributed new insights into comparisons of dose response between Hiroshima and Nagasaki.

Through the Beebe Fellowship, Dr. Pawel returned to work at RERF from September to December of 2003. “I decided to work on a problem relating to the estimation of site-specific cancer risks,” explained Dr. Pawel. His interest stemmed in part from a talk given by Dr. Donald



David Pawel

Pierce, who noted that among women the fitted site-specific mortality risks for solid cancers (1950–90) did not vary significantly by cancer site. During the Beebe Fellowship, Dr. Pawel was able to show that simple “shrinkage estimates” may improve estimates of site-specific risks derived from cancer incidence data among atomic bomb survivors.

From February through April 2004, Dr. Pawel split his time between EPA and NCI. At NCI, he worked with **Charles Land, Ph.D.** (REB), to investigate the feasibility of applying his RERF work to improve a computer program that calculates radiogenic risks. “I enjoyed very much working at NCI, and though I still have much to do on this project, I look forward to a continued collaboration with REB,” said Dr. Pawel.

The Beebe Fellowship is sponsored by the Department of Energy, National Academy of Sciences, NCI, and RERF. It is intended for mid- to senior-level epidemiologists or biostatisticians and allows great flexibility in working arrangements. More information can be found at <http://dceg.cancer.gov/radia-gilbertbeebeFellowship.html>. ■

—Maria Sgambati, M.D.



Maria Sgambati

During her tenure as editor, circulation grew and the newsletter improved in content and appearance while providing interesting highlights of the science and staff of DCEG.

ARRIVEDERCI A MARIA

Maria Sgambati, M.D. (OD), editor of *Linkage*, has transferred to the Division of Cancer Prevention as a Program Director in the Community Oncology and Prevention Trials Research Group. In her new job, she will work with the Community Clinical Oncology program, which coordinates the conduct of NCI-funded clinical trials in community practices. Since 2002, Dr. Sgambati has been the managing editor of *Linkage* and performed various other writing and editing tasks. Before that she was a clinical research fellow in GEB.