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DCEG
Division of Cancer Epidemiology and Genetics

Linkage

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DIRECTOR'S PAGE

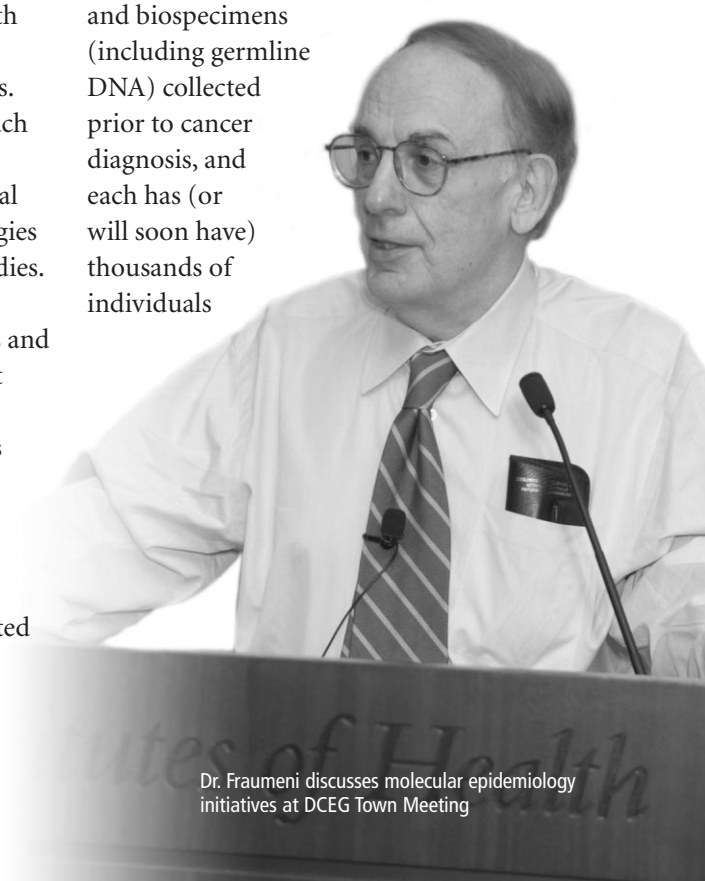
Molecular Epidemiology: A Time for Strategic Partnerships

Epidemiology has been depicted as a scientific approach that moves slowly but with great force. By incorporating the powerful new tools being generated by recent advances in genomics and molecular sciences, however, epidemiology has an unparalleled opportunity to move more quickly and with greater force than ever. To foster this approach, NCI has designated molecular epidemiology a strategic priority area for meeting the Director's 2015 challenge goal. Poised to accelerate knowledge about the genetic and environmental components of cancer induction and progression, it will also help identify new preventive, diagnostic, and therapeutic interventions.

An integral feature of this initiative is planning and developing strategic partnerships that link epidemiologists with one another and with genomicists and other investigators from the clinical, basic, and population sciences. This transdisciplinary team-based approach responds to a growing consensus in the scientific community that the full potential of genomic and other emerging technologies will require large-scale epidemiologic studies.

Study designs should have the efficiencies and power to identify common low-penetrant susceptibility genes and their interactions with exogenous or endogenous exposures gleaned from questionnaires and biospecimen collections. This can be accomplished through consortia that combine the resources of several cohort and/or case-control studies in a coordinated approach that enables rapid replication of positive findings using independent datasets. This strategy avoids the cumbersome and expensive trial-and-error process that now occurs when false-positive findings from individual studies appear in the literature. When reproducible findings emerge in the consortia, pooling of datasets provides the statistical power to quantify the risks associated with specific gene variants and exposures and to enable subset analyses that uncover gene-gene and gene-environment interactions.

One such unique partnership is the *Consortium of Cohorts*, an international collaboration of intramural and extramural investigators responsible for 23 independently funded population cohorts encompassing 1.2 million individuals. Each cohort has extensive information on known or suspected risk factors and biospecimens (including germline DNA) collected prior to cancer diagnosis, and each has (or will soon have) thousands of individuals



Dr. Fraumeni discusses molecular epidemiology initiatives at DCEG Town Meeting

DCEG *Linkage*

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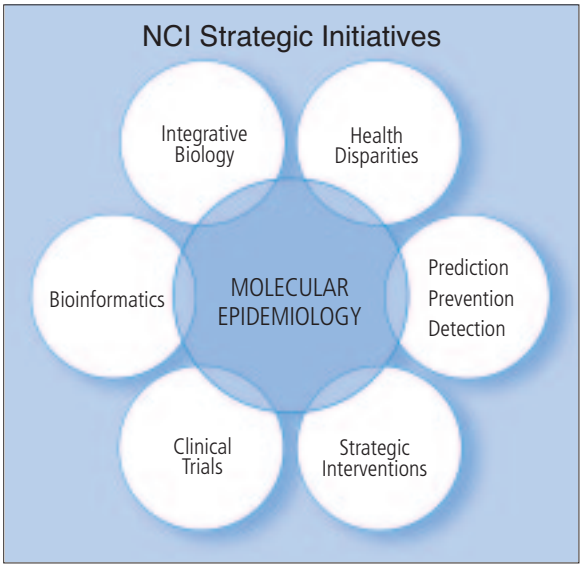
who have developed cancer. Through a joint planning process, this consortium provides an integrative framework for nested case-control studies of specific cancers arising within the cohorts to systematically evaluate molecular and biochemical biomarkers of susceptibility and early-stage disease.

Last February, consortium members met at NIH to discuss progress and future directions. A status report was given for an initial study conducted among 600,000 individuals in 10 cohorts that have the largest number of cancer cases. This study focuses on the risk of breast cancer (7,000 cases) and prostate cancer (9,000 cases) associated with variations in hormone- and growth-factor-related genes and their interactions with risk factor data and circulating levels of hormones and growth factors. The meeting also provided an opportunity to discuss new high-throughput genotyping technologies that can be used for candidate gene approaches and genome-wide searches as well as linkage-based studies. This discussion was informed by a presentation by Dr. Francis Collins, Director of the Human Genome Research Institute, on the status of the International HapMap Project, which holds promise as a research tool for future studies in genetic and molecular epidemiology.



Other types of strategic partnerships are under development, including international *case-control consortia* that involve investigators responsible for population- or hospital-based case-control studies, with special attention to less common cancers that cannot be easily evaluated in cohort studies. Intramural and extramural investigators have already joined forces in a coordinated series of ongoing case-control studies on non-Hodgkin's lymphoma and brain tumors. In addition, several scientists interested in familial cancer have formed international *family-based consortia.* Current emphasis is on familial syndromes in which high-penetrant genes have eluded discovery, or where opportunities exist to identify genetic and environmental modifiers of inherited risk. The most recent intramural/extramural partnership of this kind centers on studies of familial chronic lymphocytic leukemia.

Many complex scientific, administrative, and cultural challenges are involved in developing these team-based transdisciplinary partnerships, which seemingly run counter to the traditional model of individual investigators or groups that work independently. The two strategies are really complementary and synergistic, however, speeding the discovery of causal agents and pathways, early-detection markers, and interventions designed to prevent and control cancer. ■

—Joseph F. Fraumeni, Jr., M.D.

[This article appeared in the February 24th issue of the NCI *Cancer Bulletin*]

RISK PREDICTION MODELS WORKSHOP SETS GOALS

Estimating absolute risk of cancer can have profound implications for targeted prevention strategies and clinical decision making. On May 20, more than 100 experts met in Washington, DC, for a workshop about cancer risk prediction models. "This interdisciplinary workshop broke ground by bringing together the cancer risk prediction modeling community for the first time and helping identify the research steps needed to move this field forward," noted Andrew Freedman, Ph.D., cochair of the workshop from NCI's Division of Cancer Control and Population Sciences (DCCPS). The workshop was cosponsored by NCI's Division of Cancer Epidemiology and Genetics (DCEG), DCCPS, and the NCI Office of Women's Health.

The workshop included four sessions on risk prediction models: applications, development and implementation, evaluation and validation, and predicting germline mutation carrier status. Poster sessions presented models in use or under development, including models for melanoma and breast, lung, colorectal, and prostate cancer, and for genetic susceptibility to colorectal and breast cancer. As noted by DCEG's

Cancer Risk Prediction Workshop Planning Committee: Ruth Pfeiffer, Mitchell Gail, Daniela Seminara, Andrew Freedman, and Rachel Ballard-Barbash (not pictured: Patricia Hartge and Graham Colditz)

Ruth Pfeiffer, Ph.D., cochair of the workshop, "After intensive discussions between model developers and clinicians, there was consensus that model performance should be judged in the context of specific applications and that further methodological research is needed to develop criteria for model assessment."

Priorities for future research include identifying cancer sites for which new risk prediction models are useful, finding ways to improve current and future cancer risk prediction models by incorporating new clinical and biological markers, and providing data resources and study populations for modeling and validation. "The meeting was valuable in describing useful applications for risk models with modest discriminatory power and applications such as screening for which more discriminating risk models are needed," said DCEG's **Mitchell Gail, M.D., Ph.D.**, who 15 years ago developed a widely used breast cancer risk prediction model. ■

Jim Vaught and Nathaniel Rothman

DCEG HOLDS MOLECULAR EPIDEMIOLOGY COURSE

This winter, approximately 45 DCEG staff members participated in a 50-hour Molecular Epidemiology Course that was held weekly, from January through April 2004. The course, intended primarily for DCEG and Core Genotyping Facility (CGF) tenure-track investigators, staff scientists, and fellows, has become a regular part of DCEG's educational activities. "The goal of the course is to train junior research staff in the design, implementation, management, and analysis of molecular epidemiology studies within the NCI," said **Demetrius Albanes, M.D.**, Chief of DCEG's Office of Education (OE). The course also deals with how to collaborate effectively with the CGF and other laboratories.

In addition to didactic sessions and laboratory visits, students are asked to integrate methodological and analytical components into the preparation and presentation of a concept that is based on course material. Students are encouraged to seek funding for these proposals. DCEG first offered the Molecular Epidemiology Course in 2000. **Nathaniel Rothman, M.D.** (Occupational and Environmental Epidemiology Branch), and **Jim Vaught, Ph.D.** (Office of the Director), served as the backbone for this year's course. Participants benefited from their careful planning, contributions during each session, and insightful evaluations of concept proposals at the end of the session. **Kristin Kiser, M.H.A.** (OE), also provided coordination for the course.

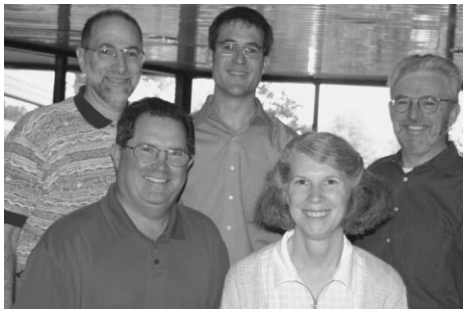
STUDY FINDS A LINK BETWEEN FORMALDEHYDE AND LEUKEMIA

Recent data from a DCEG study of industrial workers found an association between formaldehyde exposure and leukemia. The study, published in the *Journal of the National Cancer Institute*, showed that workers exposed to high peak levels of formaldehyde had a 3.5-fold increased risk of dying from myeloid leukemia compared to workers exposed to low peak levels. Leukemia risk also rose with average exposure intensity and duration, though to a lesser extent. "This analysis addressed the unresolved question of whether formaldehyde is a human carcinogen," said **Aaron Blair, Ph.D.**, senior author of the paper and Chief of the Occupational and Environmental Epidemiology Branch (OEEB).

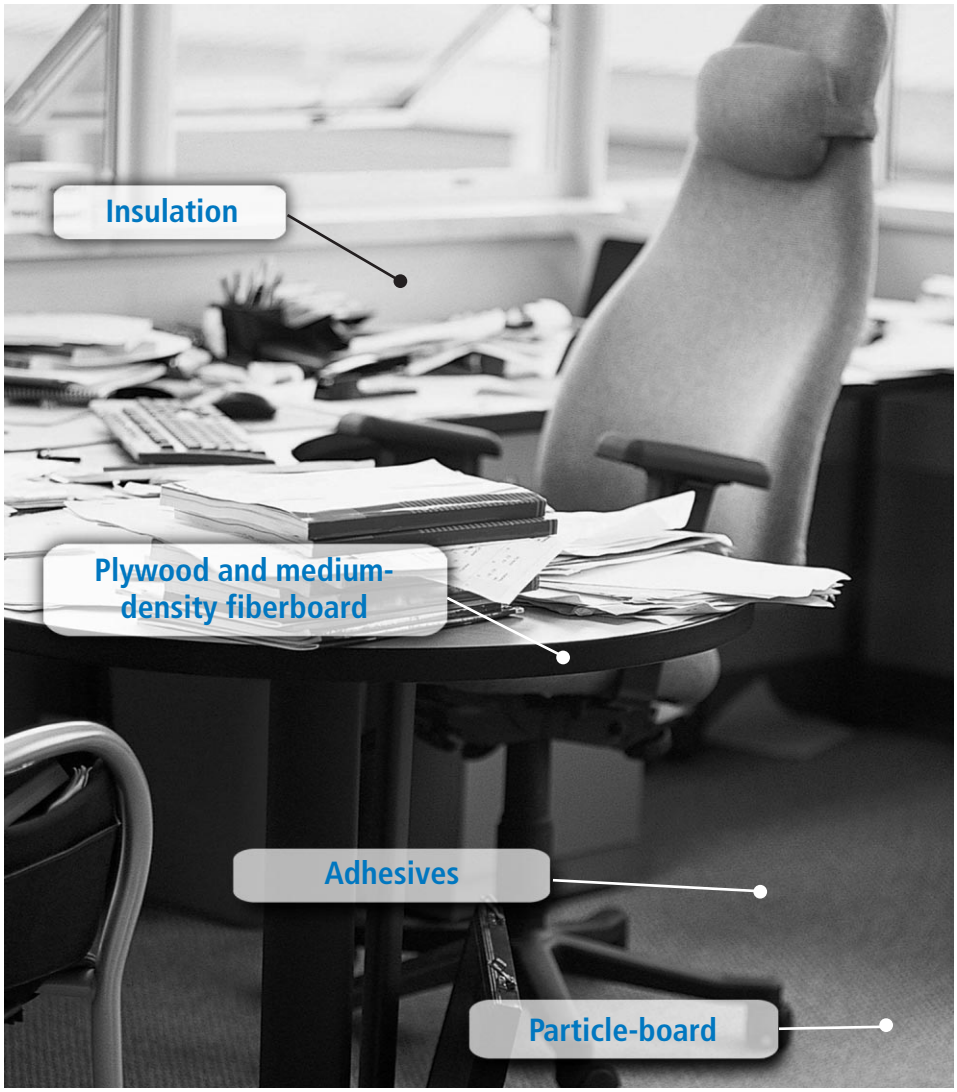
The study followed a cohort of 25,619 persons employed prior to January 1966 and through December 1994 at one of 10 U.S. industrial plants. The cohort, assembled in the 1980's, is the largest study of industrial workers exposed to formaldehyde. Formaldehyde is a flammable and colorless gas used in the production of many important commercial products, including resins, molding compounds, photographic film, textiles, decorative laminates, and plywood. It is also used as a bactericide and a tissue preservative. The U.S. National Institute for Occupational Safety and Health estimated that 1.5 million U.S. workers were exposed to formaldehyde from 1981 to 1983.

The exposure assessment, led by **Patricia Stewart, Ph.D.**, industrial hygienist and senior investigator in the OEEB, enabled the researchers to look at peak exposure, average exposure intensity, cumulative exposure, and exposure duration. "Having four metrics of exposure was a unique feature of this study," said **Michael Hauptmann, Ph.D.**, lead author of the paper and tenure-track investigator in the Biostatistics Branch. "Examining different exposure variables helped us get a fuller and more accurate picture." Data were also gathered on exposure to many other widely used chemicals in the plants.

Although formaldehyde's leukemia-inducing mechanisms are unclear, there have been reports that such exposure may cause micronuclei, DNA protein crosslinks, sister chromatid exchanges, and chromosomal aberrations in human peripheral lymphocytes. In addition, previous studies of professional groups such as embalmers, pathologists, and anatomists have suggested an association



DCEG Formaldehyde Research Team: (front) Aaron Blair and Patricia Stewart; (back) Jay Lubin, Michael Hauptmann, Richard Hayes



Although occupational formaldehyde exposures have declined, formaldehyde is still used in the production of many commercial products such as resins in woods and plastics.

with leukemia, but these studies lacked detailed exposure assessments. DCEG researchers are currently evaluating data from a nested case-control study of leukemia among embalmers with quantitative exposure assessment. At issue is whether formaldehyde is capable of reaching leukemia target cells, so NCI investigators are considering studies to evaluate genetic and epigenetic changes in blood samples from formaldehyde-exposed populations. "Molecular alterations in the peripheral blood cells of such groups will provide important evidence on whether there is a causal association with leukemia," said Dr. Hauptmann.

The study, published in the *Journal of the National Cancer Institute*, showed that workers exposed to high peak levels of formaldehyde had a 3.5-fold increased risk of dying from myeloid leukemia compared to workers exposed to low peak levels.

Although Drs. Blair and Hauptmann cite a few challenges with the study—such as potential exposure misclassification and lack of exposure information for 1980 to 1995—they think it is unlikely that the leukemia excess is due to a factor other than formaldehyde. This is because exposure misclassification was most likely nondifferential with respect to cause of death, only a few workers included in the study were still employed after 1980, and formaldehyde exposures have decreased substantially over the past two decades. While it is possible that the finding is due to chance, the study had a larger number of leukemia deaths for evaluation than any other investigation.

NCI investigators presented an updated analysis of solid cancers in a second paper, which appeared in the June 15, 2004, issue of the *American Journal of Epidemiology*. Important findings include increasing risks for nasopharyngeal cancer with average exposure intensity, cumulative exposure, duration of exposure, and peak exposure to formaldehyde (based on only nine deaths) and no association for lung cancer for any of the four metrics of formaldehyde exposure (based on 744 lung cancer deaths). The finding for nasopharyngeal cancer is consistent with experimental studies linking formaldehyde exposure to nasal cancer in rodents.

Although occupational formaldehyde exposures have declined, new sources of exposure exist, so delineating the health risks remains a priority. For instance, formaldehyde accounts for about two-thirds of the total hazardous air pollutant emissions from natural-gas-fired turbines, which may be used as a future power source.

In June, the International Agency for Research on Cancer upgraded formaldehyde to "carcinogenic to humans." Citing new evidence, including the above NCI research, the expert panel, which included Dr. Hauptmann, stated that the previous evaluation of formaldehyde as "probably carcinogenic to humans" was based on the smaller number of studies available at the time. The U.S. Environmental Protection Agency is also currently updating its assessment of health risks from formaldehyde exposure, and DCEG's work as well as other reports from recently updated occupational cohorts will be used in the process. ■

—Maria Sgambati, M.D.

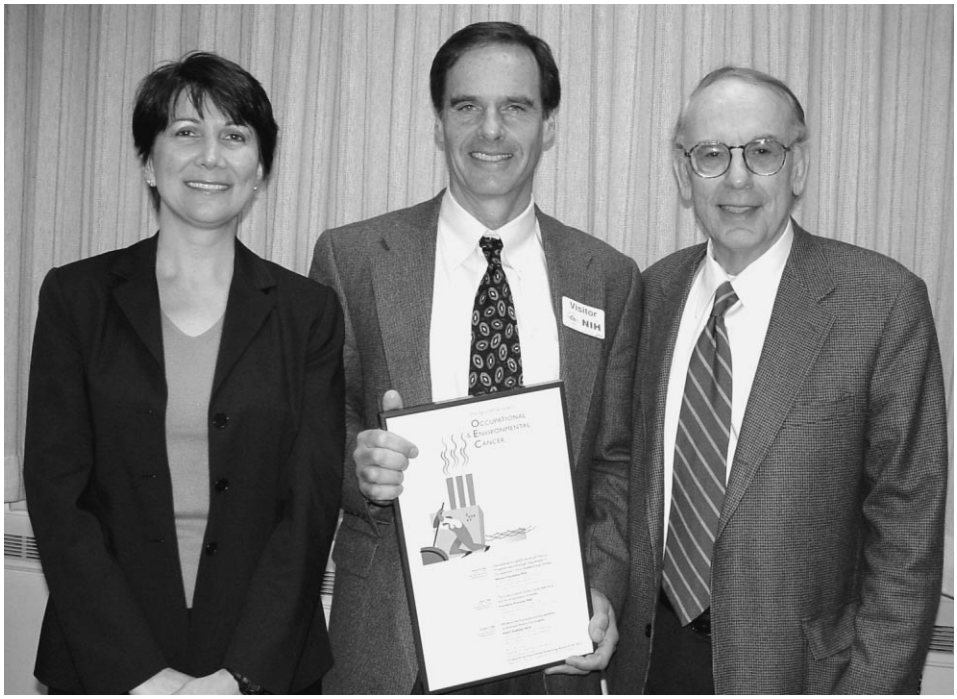
RADIATION EPIDEMIOLOGY COURSE DRAWS INTERNATIONAL AUDIENCE

Peter Inskip coordinates Radiation Epidemiology Course

Approximately 80 individuals with an interest in the health effects of radiation exposure attended a 10-day Radiation Epidemiology Course held in Rockville, MD, in May. The course, sponsored by the Radiation Epidemiology Branch (REB), attracted attendees from across the United States and around the world, including Japan, Korea, Russia, Ukraine, Belarus, Israel, Sweden, Great Britain, the Netherlands, Germany, and France. The audience included researchers, clinicians, and policymakers who represented such disciplines as epidemiology, biostatistics, basic radiation sciences, cancer biology, radiation oncology, radiation protection, and risk estimation and management. "With these diverse backgrounds and aims came diverse points of view, and most talks were accompanied by spirited discussion," said **Peter Inskip, Sc.D.** (REB), who organized the workshop. "The hope is that these interactions will help bridge the gaps between disciplines and stimulate new lines of research." The workshop addressed topics such as radiation physics and dosimetry, radiation chemistry, radiobiology and radiation oncology, and radiation epidemiology. Epidemiology discussions centered on studies of Japanese atomic bomb survivors, medically irradiated populations, and persons with occupational or environmental radiation exposures.

HARVEY CHECKOWAY VISITS AS DISTINGUISHED LECTURER

On March 25, 2004, Harvey Checkoway, Ph.D., M.P.H., visited DCEG as a Distinguished Lecturer in Occupational and Environmental Epidemiology. Dr. Checkoway is Professor of Environmental and Occupational Health Sciences at the University of Washington School of Public Health and Community Medicine, with a joint appointment in the Department of Epidemiology. He also directs the university's Superfund Basic Research Program and Training Grant in Environmental and Molecular Epidemiology, both funded by the National Institute of Environmental Health Sciences. His well-known book, *Research Methods in Occupational Epidemiology*, is one of the few epidemiologic texts that deals specifically with occupational issues. His current research ranges from studies on silica, silicosis, and lung cancer among diatomaceous earth industry workers, to environmental and genetic risk factors for Parkinson's disease, to cancer risks among textile workers in Shanghai. Dr. Checkoway's lecture addressed "Investigating straightforward and not-so-straightforward etiologic hypotheses in occupational cancer epidemiology."



Distinguished Lecture in Occupational and Environmental Cancer: Dalsu Baris, Harvey Checkoway, and Joseph F. Fraumeni, Jr.

The Occupational and Environmental Epidemiology Branch (OEEB) launched the Distinguished Lectures series in 2002. Each year, three or four prominent scientists visit for two days to give lectures and meet with DCEG staff to discuss issues and challenges of mutual interest. The objectives of the series are to expand and intensify contacts between intramural and extramural investigators, provide an opportunity for junior staff to meet with distinguished scientists, and highlight research opportunities in occupational and environmental cancer. "Having these eminent scientists as guest lecturers has been a great privilege for the OEEB and DCEG," said **Dalsu Baris, M.D., Ph.D.**, organizer of the 2004 series. "We have had stimulating discussions with them through meetings and seminars and have immensely benefited from their knowledge, experience, and wisdom."

For more information on DCEG's Distinguished Lecture series, please visit *http://dceg.nci.nih.gov/occu-DistinguishedLectures.html.* ■

MIMI YU RECOGNIZED FOR HER CONTRIBUTIONS TO DCEG

Dr. Mimi Yu, a professor in the Department of Epidemiology at the University of Southern California School of Medicine, received a DCEG Special Recognition Award in March 2004. The award was given in appreciation for Dr. Yu's many contributions to the Division while serving on the NCI Board of Scientific Counselors from 1998 to 2003. In addition to the usual heavy workload of site visits, she also chaired the advisory group for the Breast Implant Study and the Data Safety Monitoring Board for the Shandong Intervention Trial, which focused on delaying progression of precancerous gastric lesions. Dr. Yu's expertise and dedication were crucial to ensuring that these studies were conducted according to the highest standards.

Mimi Yu receives Special Recognition Award

DCEG LAUNCHES VISITING SCHOLARS PROGRAM

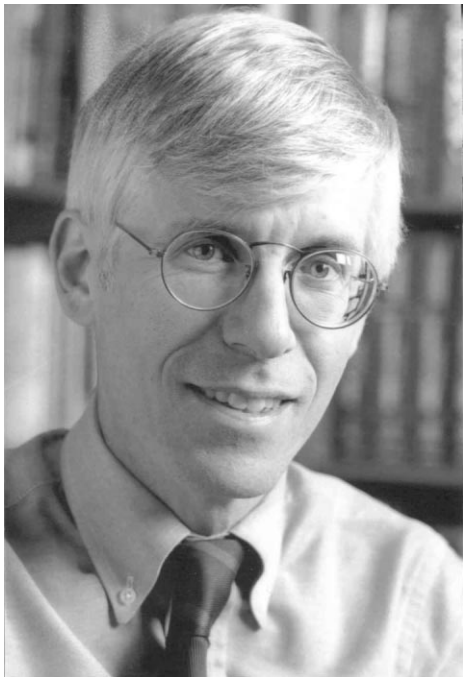
To bring leaders in the field of cancer epidemiology and genetics to NCI to share their expertise with scientific staff, DCEG created the Visiting Scholars Program (VSP), which was launched this spring. The program is structured around intensive two-day visits by world-class scientists from the extramural community and includes a special Scholar Seminar and round-robin visits with DCEG programs and branches. In addition to stimulating new ideas and research directions, the VSP will also focus on career development for young investigators in keeping with the priority that DCEG and NCI give to high-quality research training. Program goals include fostering and reinforcing creative research approaches that enhance the intramural and collaborative research portfolio of DCEG and contribute to NCI and NIH strategic priorities.

"We are pleased to honor these scientists for their accomplishments in epidemiology and public health. Their visits also expose our scientific staff to cutting-edge research that is taking place outside NIH," said DCEG Director **Joseph F. Fraumeni, Jr., M.D.**

The program was inaugurated March 17 with the visit of Dr. Elio Riboli, Chief of the Unit of Nutrition and Cancer at the International Agency for Research on Cancer in Lyon, France. During his seminar, "A multifactorial approach to cancer etiology," Dr. Riboli discussed several global issues in the field of cancer epidemiology, including recent analyses from the European Prospective Investigation into Cancer (EPIC) study. Thematic breakout sessions included a meeting with DCEG investigators to discuss the consortium approach to cancer epidemiology and an exposure-assessment working group meeting with a nutrition focus. An open-forum Meet-the-Scholar session explored new research directions, opportunities for collaborative work, and career development issues. Dr. Riboli also toured the NCI Core Genotyping Facility at the Advanced Technology Center.

On May 10 and 11, DCEG hosted Dr. Jonathan Samet, Chair of the Epidemiology Department at the Johns Hopkins Bloomberg School of Public Health. Dr. Samet spoke on "The challenge of epidemiologic research: Continued lessons from lung cancer." Breakout sessions focused on lung cancer research initiatives involving DCEG and training programs in specialized areas of epidemiology. Dr. Samet lunched with fellows during a Meet-the-Scholar session, during which the conversation focused on postfellowship career opportunities, the changing face of epidemiology, including the emerging role of large-scale studies and consortia, and the importance of grant-writing experience. A forum on "Epidemiology training in an era of subspecialization" dealt with additional potential training collaborations with Johns Hopkins and teaching opportunities. The visit culminated with the development of a Graduate Training Partnership memorandum of understanding between DCEG and the Johns Hopkins Department of Epidemiology. ■

—Demetrius Albanes, M.D.



Jonathan Samet Visits DCEG

"We are pleased to honor these scientists for their accomplishments in epidemiology and public health. Their visits also expose our scientific staff to cutting-edge research that is taking place outside NIH," said DCEG Director Joseph F. Fraumeni, Jr., M.D.

TOWN MEETING RECOGNIZES STAFF ACHIEVEMENTS

More than 30 DCEG staff members received special recognition at the Division's annual town meeting in April. During the open discussion period, DCEG Director **Joseph F. Fraumeni, Jr., M.D.**, talked about the challenges and opportunities facing DCEG and NCI and noted that research across the Division is "humming" despite budgetary constraints. Dr. Fraumeni emphasized the central role played by DCEG in developing strategic partnerships through research consortia, along with the Visiting Scholars Program, which is stimulating new ideas. In discussing the "power to convene" at NIH, Dr. Fraumeni underscored the opportunity to bring together various groups to address scientific issues through workshops and multicenter evaluations.

Shelia Zahm, Sc.D., DCEG Deputy Director, served as emcee of the award ceremony, which began with the 2003 Combined Federal Campaign (CFC) award. Under the excellent leadership of DCEG Coordinator **Elyse Wiszneauckas**, Office of the Director (OD), the Division received its sixth CFC Presidential Award and met 143 percent of its dollar goal. Recognition also went to Branch key workers: **Holly Brown**, Biostatistics Branch (BB); **Patricia Chandler**, Office of Division Operations and Analysis (ODOA); **Natacha Charles**, Clinical Genetics Branch (CGB); **Jennifer Connor**, Hormonal and Reproductive Epidemiology Branch (HREB); **Michelle Fitzpatrick**, Administrative Resource Center (ARC); **Julie Russell Grey**, Viral Epidemiology Branch (VEB); **Wen-Yi Huang, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB); **Ursula Leitzmann, M.A.**, Radiation Epidemiology Branch (REB); **Sandy Rothschild**, (OD); **Tawanda Roy**, Nutritional Epidemiology Branch (NEB); and **Rashida Williams**, Genetic Epidemiology Branch (GEB).

Joseph F. Fraumeni, Jr. (far left) with DCEG CFC keyworkers (from left to right): Natacha Charles, Julie Russell Grey, Elyse Wiszneauckas (coordinator), Jennifer Connor, Michelle Fitzpatrick, Patricia Chandler, Wen-Yi Huang

Sam Mbulaiteye and Michael Hauptmann receive Outstanding Research Paper of 2003 by Fellows Award (not pictured: Ulrike Peters)

Three fellows received awards for Outstanding Research Paper, which recognizes publications by fellows during the past calendar year that demonstrated impact, innovation, and clarity of thought and language. **Michael Hauptmann, Ph.D.** (BB), was recognized for his paper, "Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries," published in the *Journal of the National Cancer Institute;* **Sam Mbulaiteye, M.D.** (VEB), for his paper, "Human herpesvirus 8 infection and transfusion history in children with sickle-cell disease in Uganda," also published in the *Journal of the National Cancer Institute;* and **Ulrike Peters, Ph.D.** (NEB), for her paper, "Dietary fiber and colorectal adenoma in a colorectal cancer early detection program," published in *Lancet*. The staff scientist Outstanding Research Paper award went to Dr. Huang for her paper, "Alcohol

Wen-Yi Huang receives Outstanding Research Paper of 2003 by a Staff Scientist Award

Donna Gellerson receives Special Recognition Award

concentration and risk of oral cancer," published in the *American Journal of Epidemiology*.

Three postdoctoral fellows received the DCEG Fellowship Achievement Awards for outstanding productivity: **Lifang Hou, M.D., Ph.D.** (OEEB), **Tania Mara Welzel, M.D., Ph.D.** (VEB), and **Rose Yang, Ph.D.** (GEB). The winners receive a two-step annual increase in their NCI fellowship stipend.

This year, the Division selected four individuals to receive Special Recognition Awards. **Betty Jane (B.J.) Stone, Ph.D.** (BB), was honored for exemplary service and meticulous work as Chair of the Technical Evaluation of Questionnaires Committee. **Nathaniel Rothman, M.D.** (OEEB), and **Jim Vaught, Ph.D.** (OD), were recognized for organizing the DCEG Molecular Epidemiology Course, and **Donna Gellerson** (ARC) was honored for extraordinary work as manager of the DCEG Administrative Resource Center.

The Outstanding Mentor Award honors scientists who demonstrate exceptional skill in and commitment to training and mentoring. **Mark H. Greene, M.D.** (CGB), was recognized by fellows for being an "outstanding scientist, collaborator, and mentor" and for "encouraging creativity and innovation and serving as a role model for all young investigators." **Rashmi Sinha, Ph.D.** (NEB), was also honored for her ability to "guide fellows through complex scientific issues and to ensure a productive and rewarding training experience." **Betsy Duane-Potocki** (OD) was recognized for her work in mentoring a long line of communications interns. Under her guidance, interns "grow in their communications skills, in confidence, and in understanding of our research enterprise."

Finally, Exemplary Service Awards went to **Susan Devesa, Ph.D.** (BB), and **Neil Caporaso, M.D.** (GEB), for their sustained research accomplishments and outstanding service to the Division. Dr. Devesa was cited for her pivotal role in analyzing and interpreting descriptive data on cancer incidence and mortality and in directing the development of the U.S. Atlas of Cancer Mortality. She is an invaluable consultant, collaborator, and mentor to scientists across the Division and NCI. Dr. Caporaso was cited for unselfish participation on numerous committees, including the DCEG Biorepository Review Group, the DCEG Molecular Epidemiology Committee, and several NCI committees and working groups addressing tobacco-related research. At the same time, he has conducted state-of-the-art research on gene-environment interactions in lung cancer and has spearheaded creation of an international consortium of researchers involved in the study of familial chronic lymphocytic leukemia. ■

DCEG FELLOWS AWARDED DOCTORAL DEGREES

Congratulations to two DCEG fellows who recently received doctoral degrees. **Preetha Rajaraman, Ph.D.**, of the Radiation Epidemiology Branch (REB), completed her doctoral degree through the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health. Her dissertation research focused on occupational exposure to lead, genetic susceptibility, and risk of brain tumors in adults, and was completed under the mentorship of **Peter Inskip, Sc.D.** (REB), and **Patricia Stewart, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB). Dr. Jonathan Samet of Johns Hopkins was her faculty advisor.

Elizabeth Brown, Ph.D., of the Viral Epidemiology Branch (VEB), successfully defended her doctoral thesis, which was also completed through the Department of Epidemiology at Johns Hopkins. Her dissertation research, "Human herpesvirus-8 and classical Kaposi sarcoma in an Italian case-control study," focused on phenotypic and genotypic markers of immunity. **James Goedert, M.D.** (VEB), **Stephen Chanock, M.D.**, of NCI's Core Genotyping Facility, and Dr. Anthony Alberg of Johns Hopkins were her mentors.

Drs. Brown and Rajaraman will continue to work in DCEG as postdoctoral fellows. In addition to graduation ceremonies at Johns Hopkins, they also participated in the annual Certificate Award Ceremony for graduate students at NIH and in the first NIH Graduate Student Symposium Day. Dr. Rajaraman was one of nine NIH graduate students selected to give an oral presentation on her dissertation research project, and Dr. Brown gave a poster presentation.

Other DCEG graduate students who gave poster presentations at the symposium included **Sadie Hutson, Ph.D., C.R.N.P.** (Clinical Genetics Branch), on "The experiences of siblings of patients with Fanconi's anemia," and **Hormuzd Katki, M.S.** (Biostatistics Branch), on "Extending Mendelian mutation prediction models to handle errors in reported family history."

Graduate students from more than 50 universities who were completing doctoral research at NIH took part in the symposium. The daylong event also featured distinguished speakers, including Dr. Harold Varmus, NIH director from 1993 to 1999 and currently president of Memorial Sloan-Kettering Cancer Center in New York. In addition to showcasing graduate student research at NIH, outstanding mentors were honored. ■

Preetha Rajaraman speaks at NIH Graduate Student Symposium


Elizabeth Brown receives certificate from Michael Gottesman, Deputy Director for Intramural Research, NIH

CULTURAL CONSIDERATIONS WORKSHOP HELPS RAISE AWARENESS

People come from all over the world to work in DCEG, NCI, and NIH. The gathering of individuals from diverse places and backgrounds creates a rich intellectual environment but can also cause communication problems due to cultural differences that lead to misunderstandings. Key stumbling blocks in communication across cultures include language differences, assumptions of similarities, and nonverbal patterns. Intercultural communication skills can help people better understand those who think and behave differently through reconciling conflicting values to create shared meaning.

Ursula Leitzmann teaches workshop on cultural considerations in career development

To build and sustain an effective and successful work environment, DCEG offers a series of Cultural Considerations Workshops. Initially targeted at DCEG international fellows, the workshops have been made available to other DCEG staff and fellows in NCI's Center for Cancer Research. Led by intercultural trainer **Ursula Leitzmann, M.A.**, of the Radiation Epidemiology Branch, the workshops introduce individuals to the concepts of cultural awareness and communication. Attendees learn to understand the visible aspects of culture, such as behavior, and underlying beliefs and values—the less visible aspects of culture. Special attention is given to American cultural values, such as the preference for task orientation and individual achievement. In the workshops, intercultural skills are strengthened through a series of case studies. ■

I-131 COMMUNICATIONS AID WINS PLAIN LANGUAGE AWARD


Betsy Duane-Potocki (third from left) and other collaborators receive NIH Plain Language Award for I-131 communications aid from Elias Zerhouni (far left) and Andrew von Eschenbach (far right) (not pictured from DCEG: Andre Bouville) *(Photograph Credit: Mark Waldo)*

Betsy Duane-Potocki (Office of the Director) and **Andre Bouville, Ph.D.** (Radiation Epidemiology Branch), were part of a group of collaborators who received an NIH Plain Language Award in May. The group won for its work on a flip chart that is part of a series of communications materials developed to provide information for Americans exposed to I-131 (a form of radioactive iodine) through fallout from aboveground nuclear testing in the 1950's and early 1960's. The flip chart, which received an award in the "Outstanding" category, targets Native Americans and is designed to help community leaders and healthcare professionals address concerns about I-131 exposure and thyroid cancer. Margaret Farrell, M.P.H., R.D., in the NCI Office of Communications, led the project. More information about the NIH I-131 communications materials can be found at *http://cancer.gov/i131*.

NIH launched the Plain Language Initiative in 1999, following a White House memorandum calling for clearer writing throughout the Federal government. Plain language documents should have logical organization and easy-to-read design features and use personal pronouns, short sentences, and common, everyday words.

DCEG SCIENTISTS HONORED WITH DEPARTMENTAL SERVICE AWARDS

Two DCEG scientists have been selected to receive the 2004 Department of Health and Human Services (DHHS) Secretary's Award for Distinguished Service. **Robert Hoover, M.D., Sc.D.**, and **Shelia Zahm, Sc.D.**, were the only two NCI nominees chosen by DHHS Secretary Tommy Thompson for this honor. Individuals are selected for outstanding abilities, leadership skills, and exceptional contributions to the Department's mission. Secretary Thompson will present the awards on July 14.

Dr. Hoover, who directs DCEG's Epidemiology and Biostatistics Program, was cited for pioneering research in identifying environmental and genetic determinants of cancer and for his enduring contributions to epidemiology and public health. His personal research on hormones and cancer included the first study linking hormone replacement therapy to breast cancer and the most comprehensive study of women exposed to diethylstilbestrol and their children. He has also directed a wide-ranging multidisciplinary epidemiology program covering virtually every cancer and risk factor. Widely recognized as one of the nation's leading cancer epidemiologists, Dr. Hoover is an outstanding methodologist and a major force behind the recently created NCI Consortium of Cohorts, which will help clarify the role of environmental and genetic factors and their interactions in cancer etiology.

Two DCEG scientists have been selected to receive the 2004 Department of Health and Human Services (DHHS) Secretary's Award for Distinguished Service. Robert Hoover, M.D., Sc.D., and Shelia Zahm, Sc.D., were the only two NCI nominees chosen by DHHS Secretary Tommy Thompson for this honor.

Robert N. Hoover and Shelia H. Zahm receive DHHS Distinguished Scientist Awards

Dr. Zahm, who is Deputy Director of DCEG, was cited for her leadership and coordination of national research programs in environmental and occupational cancers, including major initiatives to evaluate the relationship of exposures to cancer and to investigate the risk of occupational cancer among women. She has played a key role in sustaining and strengthening a highly collaborative program of epidemiologic and interdisciplinary research into the environmental and genetic determinants of cancer. In addition to her crucial role in helping shape and manage the Division's research programs, Dr. Zahm has devoted a significant amount of time to a wide variety of scientific management responsibilities, such as chairing the panel to oversee the Chornobyl Research Program upon its transfer to DCEG. ■

SUMMER STUDENTS WIN EPIDEMIOLOGY AWARDS

Two high school students who participated in DCEG's 2003 summer research program were recently selected to receive a Young Epidemiology Scholar (YES) award sponsored by the Robert Wood Johnson Foundation and the College Board. **Chuankai Michael Pan**, a senior at Winston Churchill High School in Potomac, MD, was selected as a regional finalist for his work on "Smoking and passive smoking in relation to gallstone disease among women in Shanghai, China." Mr. Pan's mentors were **Wong-Ho Chow, Ph.D.**, and **Bu-Tian Ji, M.D., Dr.P.H.**, of the Occupational and Environmental Epidemiology Branch. Mr. Pan will soon return to DCEG for a summer internship to continue his analysis of gallstone disease and smoking. In the fall he will attend the University of Pennsylvania.

Tian Yang, a senior from Montgomery Blair High School in Silver Spring, MD, was also selected as a regional finalist. Mr. Yang worked in the Viral Epidemiology Branch under the guidance of **James Goedert, M.D.** His project examined the effects of acetaminophen and nonsteroidal anti-inflammatory drug use among hemophiliacs. In the fall, Mr. Yang will attend Carnegie Mellon University in Pittsburgh.

The Robert Wood Johnson Foundation and the College Board sponsor the YES competition to inspire talented high school students to investigate the many behavioral, biological, environmental, and social factors that affect health, and to identify ways to improve public health. The competition offers college scholarship awards to high school juniors and seniors who conduct outstanding research projects that apply epidemiologic methods of analysis to a health-related issue.

Michael Pan wins Young Epidemiology Scholar Award

The Robert Wood Johnson Foundation and the College Board sponsor the YES competition to inspire talented high school students to investigate the many behavioral, biological, environmental, and social factors that affect health, and to identify ways to improve public health.

Every year, DCEG offers a summer research experience for students interested in exploring careers in cancer epidemiology, genetics, and related areas. It is open to high school, college, and graduate students, including medical and dental students. Successful applicants join the Division for at least eight weeks between May and September. Under the supervision of Division scientists, the students carry out epidemiologic projects. They are also encouraged to attend lectures offered under the NIH Summer Seminar Series, participate in DCEG seminars and meetings, and present their work at the NIH Summer Research Program Poster Day. For more information on DCEG's summer program, go to *http://dceg.cancer.gov/summer.html.* ■

MICHAEL KASTAN FINISHES BOARD TERM

In June 2004, **Michael Kastan, M.D., Ph.D.**, completed five years of service as a member of the Clinical Sciences and Epidemiology Subcommittee of NCI's Board of Scientific Counselors (BSC-1). Dr. Kastan, who is a professor and chairman of the Department of Hematology and Oncology at St. Jude's Children's Hospital in Memphis, TN, has served as chair of the BSC-1 since 2001. The BSC advises the Intramural Division Directors, along with the NCI Director and Deputy Directors, on matters concerning scientific program policy and future research directions, and evaluates the scientific productivity of the Intramural Research Program through the site visit process. As part of his BSC activities, Dr. Kastan also served on the Planning Committee for developing the FY 2003 Bypass Budget. His contributions to the Institute and to DCEG have been greatly appreciated.

Michael Kastan completes BSC term ***(Photograph Credit: Bill Branson)***

PHILIP CASTLE SEEKS ANSWERS TO CAUSES OF CERVICAL CANCER

Philip Castle, Ph.D., M.P.H., thought he was just fulfilling a degree requirement when he signed up for a physiology course while in graduate school at Johns Hopkins University. The course was a turning point, however.

"The class was incredible and very diverse…and I knew I wanted to do a lab rotation with the professor," says Dr. Castle. "His lab was studying new methods of preventing sexually transmitted diseases. That was where and when I caught my public health bug."

Before that, Dr. Castle, a native of Maine, was "more of a biologist but taking as much physics as I could because I felt I needed to understand it to be a good scientist." He doesn't see any of his education going to waste. "Every [experience], plus what I'll learn in the future, is a tool to be applied to the problem. None of it goes away, and the key is to bring it all to the table until the problem is solved."

The problem in question is preventing cervical cancer. Today, Dr. Castle—who was recently appointed as a tenure-track investigator in DCEG's Hormonal and Reproductive Epidemiology Branch—is focused on the epidemiology, prevention, and treatment of human papillomavirus (HPV) infection, the causative agent of cervical cancer. Most women are infected with HPV at some point in their lives; usually, the infection clears without incident. Rarely, the virus persists, predisposing the woman to cervical cancer. The American Cancer Society estimated that in 2003, 12,200 women in the United States were diagnosed with this type of cancer, and 4,100 died as a result. Worldwide, cervical cancer has a large impact, accounting for nearly 500,000 new cases and nearly 250,000 deaths annually.

"I like the fact that we're on the road to making a major public health impact on a worldwide cancer problem, particularly one that disproportionately affects developing countries. We have an opportunity that is very exciting— to take it [the cervical cancer field] to the next level and apply our knowledge from etiologic studies to make a difference."

After finishing his doctoral degree in biophysics, Dr. Castle joined NIH as a postdoctoral fellow at the National Institute of Diabetes and Digestive and Kidney Diseases to work on the molecular biology of the zona pellucida, the glycoprotein matrix that surrounds the mammalian egg and mediates early fertilization events. But his desire to be more immersed in etiology and public health led him to enter the NCI's Cancer Prevention Fellowship program, run by the Division of Cancer Prevention. As part of the program, Dr. Castle completed an M.P.H. degree at the Johns Hopkins Bloomberg School of Public Health. He also began working with DCEG researchers **Mark Schiffman, M.D.**, and **Allan Hildesheim, Ph.D.**, on the molecular epidemiology of HPV and cervical cancer.

"I like the molecular epidemiology perspective," the 39-year-old says. "I like the fact that we're on the road to making a major public health impact on a worldwide cancer problem, particularly one that disproportionately affects developing countries. Some might say that the HPV and cervical cancer field is very mature with not much more to do, but actually there is still plenty to learn. We have an opportunity that is very exciting—to take it to the next level and apply our knowledge from etiologic studies to make a difference."

Philip Castle

Dr. Castle is working in three areas:

1. Natural history of infection.

"In these studies, I'm trying to understand the interaction of the virus with the host, down to which cells are responsible for clearance of the infection," he says. Questions to be answered include:

- Can we measure immune responses from cervical secretions and get a whole profile of immune response?
- Which molecular factors determine whether a woman clears the infection versus the unusual event where the infection progresses to precancer or cancer?

- How do smoking and other sexually transmitted diseases other than HPV affect the risk of an increased risk of developing precancer in HPV-infected patients?

2. Evaluating methods for measuring HPV.

"Because HPV is the central cause of cervical cancer, persistent viral infection must precede getting cancer," adds Dr. Castle. "Being able to measure HPV and figure out the determinants of persistent infection—understanding this and validating the measurements—is an important part of what I do." Dr. Castle also notes that further understanding etiologic intricacies in the HPV/cervical neoplasia relationship will help refine screening and diagnostic tools and advance the fields of prevention, diagnosis, and treatment.

3. Developing interventions that target women with persistent infection.

"The obvious and most interesting tools are vaccines," he says. "I'm involved in a number of activities to evaluate the mechanisms by which vaccines might prevent infection or lead to clearance of a pre-existing infection. What happens in the genital tract when a woman is vaccinated? Is it possible to measure antibodies? Does the menstrual cycle affect antibody levels and other markers of response? What are the critical biomarkers for clearance of infection?"

According to Dr. Castle, "These three areas are so interrelated that one can't be done without the others. Eventually, we will have the tools to prevent a major form of cancer. Why not shoot for that as a career goal? It's better to swing for the fences than not to swing at all." ■

—Nancy Volkers

New WSA-Elect Debra Silverman with Lynn Goldin

DEBRA SILVERMAN IS NEW WOMEN SCIENTIST ADVISOR-ELECT

Debra Silverman, Sc.D., of the Occupational and Environmental Epidemiology Branch has been selected as the DCEG Women Scientist Advisor (WSA)-Elect. The WSA term is four years: two as WSA-Elect and two as the main representative. Dr. Silverman will work with **Lynn Goldin, Ph.D.**, of the Genetic Epidemiology Branch, who is the current WSA for DCEG. Many thanks go to **Rashmi Sinha, Ph.D.**, of the Nutritional Epidemiology Branch, who just finished serving as the WSA.

The NIH WSA committee is composed of more than 30 women who are principal investigators across the NIH institutes. Member responsibilities include communicating about issues with women scientists, attending NIH-wide WSA meetings, and serving on tenure-track search committees.

The NIH WSA committee is composed of more than 30 women who are principal investigators across the NIH institutes. Member responsibilities include communicating about issues with women scientists, attending NIH-wide WSA meetings, and serving on tenure-track search committees. Within DCEG, WSA advisors meet regularly with Division Director **Joseph F. Fraumeni, Jr., M.D.**, to advise him on issues relevant to women scientists. The WSAs also participate in all DCEG Senior Advisory Group meetings. Within NCI, the WSAs choose a recipient for the annual Rosalind Franklin Award given at the NCI Combined Intramural Retreat and review applications for the Sallie Rosen Kaplan Fellowship, a competitive postdoctoral position for women in cancer research. The WSAs are conducting an NCI salary analysis to determine if gender inequities exist.

SCIENTIFIC HIGHLIGHTS

BREAST CANCER

Role of Insulin Factors in Breast Pathology

Serum concentrations of insulin-like growth factor-I (IGF-I), its major binding protein (IGFBP-3), c-peptide (a marker of insulin secretion), and the ratio c-peptide:fructosamine (a marker of insulin resistance) were evaluated in relation to the risk of epithelial hyperplasia (186 subjects), localized breast cancer (185 subjects), and nonepithelial breast changes (159 subjects) among postmenopausal women. Serum concentrations of IGF-I, IGFBP-3, and the ratio IGF-I:IGFBP-3 were not related to risk of either hyperplasia or cancer. For women in the highest quartile of c-peptide or c-peptide:fructosamine compared to those in the lowest quartile, the odds ratios (ORs) for hyperplasia were 3.0 (CI = 1.4–6.5) and 3.3 (CI = 1.5–7.3), respectively (p trend = 0.02 and 0.02, respectively). The corresponding ORs for breast cancer were 1.5 and 1.6, respectively. Insulin and insulin resistance may play a role in breast pathology in postmenopausal women. **(Schairer C, Hill D, Sturgeon SR, Fears T, Pollak M, Mies C, Ziegler RG, Hoover RN, Sherman ME. Serum concentrations of IGF-I, IGFBP-3 and c-peptide and risk of hyperplasia and cancer of the breast in postmenopausal women. *Int J Cancer* 2004;108:773-9)**

Familial Breast Cancer Risk and Polymorphisms in DNA repair and *BRCA1* -related Genes

Polymorphisms in DNA repair genes can impact protein function leading to genomic instability facilitated by growth stimulation and increased cancer risk. Nineteen single nucleotide polymorphisms (SNPs) in eight genes involved in base excision repair (*XRCC1*, *APEX*, *POLD1*), BRCA1 protein interaction (*BRIP1*, *ZNF350*, *BRCA2*), and growth regulation (*TGFss1*, *IGFBP3*) were evaluated. Using the kin-cohort method, breast cancer risk for ages 50 and 70 was estimated from family cancer history data collected from a series of breast cancer cases (n = 748) identified in a cohort of female U.S. radiologic technologists. Among 2,430 female first-degree relatives of cases, 190 breast cancers were reported. Genotypes associated with increased risk were *XRCC1* R194W (WW and RW vs. RR, cumulative risk up to age 70, risk ratio (RR) = 2.3; CI = 1.3–3.8), *XRCC1* R399Q (QQ vs. RR, cumulative risk up to age 70, RR = 1.9; 1.1–3.9), and *BRIP1* (or *BACH1*) P919S (SS vs. PP, cumulative risk up to age 50, RR = 6.9; 1.6–29.3). The risks for those heterozygous for *BRCA2* N372H and *APEX* D148E were significantly lower than risks for homozygotes of either allele, and these were the only two results that remained significant after adjusting for multiple comparisons. Some variants in genes within DNA repair pathways and BRCA1 interacting proteins may play a role as low-penetrance breast cancer risk alleles. **(Sigurdson AJ, Hauptmann M, Chatterjee N, Alexander BH, Doody MM, Rutter JL, Struewing JP. Kin-cohort estimates for familial breast cancer risk in relation to variants in DNA base excision repair, BRCA1 interacting and growth factor genes. *BMC Cancer* 2004;4:9)**

CERVICAL CANCER

Cervical Cancer Trends by Histologic Subtype

Using data from the U.S. Surveillance, Epidemiology, and End Results (SEER) Program, incidence rates of squamous cell carcinoma (SCC) and adenocarcinoma (AC) of the cervix from 1976 to 2000 were assessed by race and disease stage to evaluate temporal changes in histologic subtypes. Among black and white women, overall incidence of invasive SCC declined over time, while the incidence of *in situ* SCC increased sharply in the 1990's. Incidence rates for AC *in situ* (AIS) also increased, especially among young women. This increase in AIS incidence in white women, however, has not yet translated into a decrease in invasive AC incidence. Among black women, invasive AC incidence rose linearly with age. Etiologic factors may explain the rising cervical AIS incidence in young white women; rising cervical AC incidence with age in black women may reflect either lack of effective screening or a differential disease etiology. Changes in screening, endocervical sampling, nomenclature, and improvements in treatment likely explain the increased *in situ* cervical SCC incidence in white and black women. **(Wang SS, Sherman ME, Hildesheim A, Lacey JV Jr, Devesa S. Cervical adenocarcinoma and squamous cell carcinoma incidence trends among white women and black women in the United States for 1976-2000. *Cancer* 2004;100:1035-44)**

COLORECTAL CANCER

Vitamin D and Risk of Colorectal Adenoma

The association of circulating vitamin D metabolites and vitamin D receptor (VDR) gene polymorphisms with advanced colorectal adenoma were studied among participants in the Prostate, Lung, Colorectal and Ovarian Cancer trial. Among cases with advanced adenoma of the distal large bowel (n = 763) and controls (n = 774), no association was seen with VDR *TaqI* polymorphism. Serum levels of 25-hydroxyvitamin D [$25_{(OH)}$D] and 1,25-dihydroxyvitamin D [$1,25_{(OH)}(2)$D] were measured in a subset of 394 cases and 397 controls. Serum levels of $25_{(OH)}$D were inversely associated with advanced adenoma risk in women but not in men; the risk for advanced adenoma decreased by 70 percent in women (highest quintile OR = 0.3; CI = 0.1–0.7) and did not

decrease in men (OR = 1.1; CI = 0.6–2.0). Among women, $25_{(OH)}D$ levels were significantly higher in current users of hormone replacement therapy than in former or never users. Serum $1,25_{(OH)}(2)D$ was not associated with advanced adenoma risk. **(Peters U, Hayes RB, Chatterjee N, Shao W, Schoen RE, Pinsky P, Hollis BW, McGlynn KA; Prostate, Lung, Colorectal and Ovarian Cancer Screening Project Team. Circulating vitamin D metabolites, polymorphism in vitamin D receptor, and colorectal adenoma risk. *Cancer Epidemiol Biomarkers Prev* 2004;13:546-52)**

ENDOMETRIAL CANCER

Insulin-like Growth Factors and Risk of Endometrial Cancer

Data from 174 women with endometrial cancer and 136 controls were analyzed to evaluate whether IGF-1, IGF-2, IGFBP-1, or IGFBP-3 were associated with endometrial cancer among postmenopausal women. Higher IGF-1 levels were not associated with endometrial cancer (OR for the highest versus the lowest tertile = 0.6; CI = 0.3–1.3). Endometrial cancer was inversely associated with IGF-2 (OR for the highest tertile = 0.4; CI = 0.2–0.7) and IGFBP-3 (OR for the highest tertile = 0.40; CI = 0.2–0.8). No association was seen for IGFBP-1. The potential role of the IGF system in endometrial proliferation and carcinogenesis warrants further research. **(Lacey JV Jr, Potischman N, Madigan MP, Berman ML, Mortel R, Twiggs LB, Barrett RJ, Wilbanks GD, Lurain JR, Fillmore CM, Sherman ME, Brinton LA. Insulin-like growth factors, insulin-like growth factor-binding proteins, and endometrial cancer in postmenopausal women: results from a U.S. case-control study. *Cancer Epidemiol Biomarkers Prev* 2004;13:607-12)**

ESOPHAGEAL CANCER

CDKN2A Mutations in Esophageal Cancer

In esophageal squamous cell carcinoma (ESCC), loss of heterozygosity (LOH) is common on chromosome 9p; genetic alterations in *CDKN2A* and *CDKN2B* on 9p are also common. To determine if these two genetic alterations are related, 56 cases of ESCC from a high-risk Chinese population were analyzed. LOH at one or more loci on chromosome bands 9p21-p22 was found in 73 percent of patients and occurred more frequently in patients with a family history of upper gastrointestinal cancer than in those without. *CDKN2A* mutations were observed in 25 percent of cases, and the LOH pattern was significantly different for individuals with and without a *CDKN2A* mutation. Three new single nucleotide polymorphisms (SNPs) and two previously reported SNPs were identified in this group of patients. Intragenic allelic loss at polymorphic sites in *CDKN2A* was detected in 32 percent of cases; 13 percent of the cases exhibited what is considered classic (n = 4) or potential (n = 3) evidence of biallelic inactivation. Only one alteration was observed in *CDKN2B*. Both mutation and intragenic allelic loss in *CDKN2A* appear to play a role in the development of ESCC. **(Hu N, Wang C, Su H, Li WJ, Emmert-Buck MR, Li G, Roth MJ, Tang ZZ, Lu N, Giffen C, Albert PS, Taylor PR, Goldstein AM. High frequency of CDKN2A alterations in esophageal squamous cell carcinoma from a high-risk Chinese population. *Genes Chromosomes Cancer* 2004;39:205-16)**

GENETICS

The SNP500Cancer Database

The SNP500Cancer Database provides sequence and genotype assay information for candidate single nucleotide polymorphisms (SNPs) useful in mapping complex diseases. The database is an integral component of NCI's Cancer Genome Anatomy Project and provides bidirectional sequencing information on a set of control DNA samples derived from 102 subjects from the Coriell Institute for Medical Research database, which represent four self-described ethnic groups—African/African American, Caucasian, Hispanic, and Pacific Rim. All SNPs are chosen from public databases and reports, and the choice of genes includes a bias toward nonsynonymous and promoter SNPs in genes that have been implicated in one or more cancers. As of July 2003, the database contains more than 3,400 SNPs, 2,490 of which have been sequenced. SNP500Cancer is an invaluable resource for investigators to select SNPs for analysis, design genotyping assays using validated sequence data, choose selected assays already validated on one or more genotyping platforms, and select reference standards for genotyping assays. The SNP500Cancer Database is freely accessible at *http://snp500cancer.nci.nih.gov/*. **(Packer BR, Yeager M, Staats B, Welch R, Crenshaw A, Kiley M, Eckert A, Beerman M, Miller E, Bergen A, Rothman N, Strausberg R, Chanock SJ. SNP500Cancer: A public resource for sequence validation and assay development for genetic variation in candidate genes. *Nucleic Acids Res* 2004;32 Database issue:D528-32)**

Using DNA from the SNP500Cancer Database, various ethnic populations were analyzed at 1,442 SNP loci to estimate gene heterozygosity. Analyses revealed consistently reduced gene diversities at SNP loci causing amino acid changes, particularly those causing amino acid changes predicted to be disruptive to protein structure. The reduction of gene diversity at these SNP loci, in comparison to SNPs in the same genes not affecting protein structure, is evidence that negative natural selection (purifying selection) has reduced the population frequencies of deleterious SNP alleles. These data suggest that slightly deleterious mutations are widespread in the human population and that estimation of gene diversity, even in a sample of modest size, can help guide the search for disease-associated genes. **(Hughes AL, Packer B, Welch R, Bergen AW, Chanock SJ, Yeager M. Widespread purifying selection at polymorphic sites in human protein-coding loci. *Proc Natl Acad Sci* 2003;100:15754-7)**

Risks of Adverse Events in Patients with Fanconi Anemia

Fanconi anemia (FA) is an autosomal recessive condition associated with bone marrow failure (BMF) leading to acute myeloid leukemia (AML), solid tumors (ST), death, or necessitating hematopoietic stem cell transplant. Among a cohort of 144 patients with FA, individualized risks of each outcome were calculated, given the presence or absence of congenital abnormalities that occur frequently in FA. Abnormal radii were significant risk factors for BMF. The cumulative incidence of BMF by age 10 varied from 18 percent in the lowest BMF risk group to 83 percent in the highest. Patients in the lowest BMF risk group were most likely to live long enough to develop AML or ST, and (conversely) patients in the highest BMF risk group were least likely to live long enough to develop AML or ST. By age 40, the cumulative incidence of ST ranged from 0.6 percent to 29 percent in the highest and lowest BMF risk groups, respectively. Abnormal radii are the strongest predictor of early BMF in FA; a congenital abnormality score separates the large majority of FA patients with normal radii into distinct prognostic groups. **(Rosenberg PS, Huang Y, Alter BP. Individualized risks of first adverse events in patients with Fanconi anemia. *Blood* 2004; Apr 1 [Epub ahead of print])**

LUNG CANCER

Residential Radon Exposure and Lung Cancer Risk

Studies of radon-exposed underground miners predict that residential radon is the second leading cause of lung cancer mortality; however, case-control studies have not provided clear evidence of an association. Data were pooled from two large case-control studies of residential radon conducted in China. Among 1,050 lung cancer cases and 1,996 controls, the odds ratio (OR) increased significantly with greater radon concentration. The OR at 100 Becquerel/cubic meter (Bq/m^3) was 1.3 (CI = 1.0–1.4). For subjects who resided in the current home for 30 years or more, the OR at 100 Bq/m^3 was also 1.3 (CI = 1.1–1.9). Long-term radon exposure at concentrations found in many homes appears to increase lung cancer risk. **(Lubin JH, Wang ZY, Boice JD Jr, Xu ZY, Blot WJ, De Wang L, Kleinerman RA. Risk of lung cancer and residential radon in China: Pooled results of two studies. *Int J Cancer* 2004;109:132-7)**

LYMPHOHEMATOPOIETIC CANCERS

Alachlor Exposure May Increase Risk of Lymphohematopoietic Cancers

Cancer incidence during 1993 to 2000 was evaluated among pesticide applicators exposed to alachlor in the Agricultural Health Study, a prospective cohort study of licensed pesticide applicators in Iowa and North Carolina. A total of 49,980 pesticide applicators were included in this analysis, including 26,510 applicators (53 percent) who reported alachlor use. Among alachlor-exposed applicators, a significant increasing trend for incidence of all lymphohematopoietic cancers was associated with lifetime exposure-days (p for trend = 0.02) and intensity-weighted exposure-days (p for trend = 0.03) to alachlor. The risks of leukemia (rate ratio [RR] = 2.8, CI = 0.7–10.9) and multiple myeloma (RR = 5.7; CI = 0.7–45.7) were increased among applicators in the highest alachlor-exposure category. **(Lee WJ, Hoppin JA, Blair A, Lubin JH, Dosemeci M, Sandler DP, Alavanja MC. Cancer incidence among pesticide applicators exposed to alachlor in the Agricultural Health Study. *Am J Epidemiol* 2004;159:373-80)**

Risk of Lymphoproliferative Tumors among Families with CLL

The spectrum of malignancies that share common genetic factors with chronic lymphocytic leukemia (CLL) and the effects of gender and age on familial risk are unknown. The Swedish Family Cancer Database was used to test for increased familial risks of CLL and other lymphoproliferative tumors. Cancer diagnoses from 1958 to 1998 were assessed in 14,336 first-degree relatives of 5,918 CLL cases and in 28,876 first-degree relatives of 11,778 controls. Relatives of cases were at significantly increased risk for CLL (relative risk [RR] = 7.52; CI = 3.63–15.56), for non-Hodgkin's lymphoma (RR = 1.45; CI = 0.98–2.16) and for Hodgkin's lymphoma (RR = 2.35; CI = 1.08–5.08). CLL risks were similar in parents, siblings, and offspring of cases, in male and female relatives, and were not affected by the cases' age at diagnosis. Anticipation was not significant. The familial component for CLL is shared with other lymphoproliferative malignancies, suggesting common genetic pathways. **(Goldin LR, Pfeiffer RM, Li X, Hemminki K. Familial risk of lymphoproliferative tumors in families of patients with chronic lymphocytic leukemia: Results from the Swedish Family-Cancer Database. *Blood* 2004; May 25 [Epub ahead of print])**

Hepatitis C Virus and Non-Hodgkin's Lymphoma

To further investigate the suspected link between hepatitis C virus (HCV) infection and non-Hodgkin's lymphoma (NHL), testing was done on serum samples from 998 women (464 NHL cases; 534 controls) from Connecticut. Approximately 2 percent of cases and 1 percent of controls tested positive for HCV. The risk of NHL associated with HCV infection appeared to be concentrated among B-cell lymphomas (B-NHL) (OR = 2.0; CI = 0.6–8.2), particularly follicular lymphoma (OR = 4.1; CI = 0.8–19.4). Although the low prevalence of HCV in this population resulted in wide CIs for the estimated association between HCV and B-NHL subtypes, this study suggests that HCV may be associated with an increased risk of B-NHL, and that this risk may vary by B-NHL subtype. **(Morton LM, Engels EA, Holford TR, Leaderer B, Zhang Y, Zahm SH, Boyle P, Zhang B, Flynn S, Tallini G, Owens PH, Zheng T. Hepatitis C virus and risk of non-**

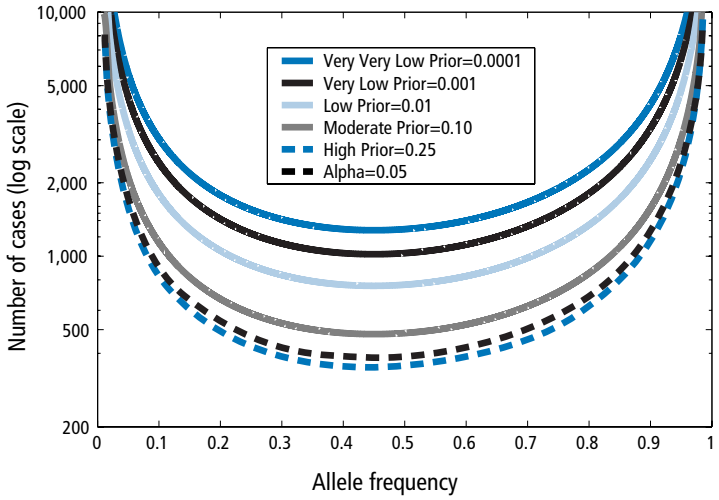


Figure 1: Sample size needed to achieve a false positive report probability (FPRP) value of 0.2 with various prior probabilities or with an α level of .05 (black broken line) for traditional sample size (N) calculations. Sample size is shown for various allele frequencies (q), with statistical power of 0.8 to detect an odds ratio of 1.5.

Hodgkin lymphoma: A population-based case-control study among Connecticut women. *Cancer Epidemiol Biomarkers Prev* 2004;13:425-30)

METHODS

Assessing the Probability that a Positive Report Is False

Too many reports of associations between genetic variants and complex diseases such as cancer are false positives, often because statistical significance is based on a *p* value alone, particularly any value below 0.05. The false positive report probability (FPRP)—the probability of no true association between a genetic variant and disease given a statistically significant finding—depends not only on the observed *p* value but also on both the prior probability that the association between the genetic variant and the disease is real and the statistical power of the test (Figure 1). FPRP can be used to decide whether a finding is not noteworthy and deserving of attention. It is shown that this approach can lead to improvements in the design, analysis, and interpretation of molecular epidemiology studies. An FPRP-based criterion can help investigators, editors, and readers of research articles protect themselves from overinterpreting statistically significant findings that are not likely to signify a true association. (Wacholder S, Chanock S, Garcia-Closas M, El Ghormli L, Rothman N. Assessing the probability that a positive report is false: An approach for molecular epidemiology studies. *J Natl Cancer Inst* 2004;96:434-42)

Risk of Human Herpesvirus-8 Infection from Transfusions

In studies of infectious disease, epidemiologists frequently estimate and compare incidence rates among different age groups, and inferences are based on cross-sectional rather than prospective data, often consisting of age at the time of study, infection status, and a chronology of events possibly associated with the disease. To understand how human herpesvirus 8 (HHV-8) is transmitted among children with sickle cell anemia in Uganda, a flexible parametric approach was developed for combining current-status data with a history of blood transfusions. Heterogeneity in transfusion-associated risk by child-specific random effects, such as host response to infection, was also modeled. An extension of the model was developed to account for the fact that the antibody assay used to detect HHV-8 status has imperfect sensitivity and specificity. These models allow the incorporation of maximum amounts of data and may improve efficiency of risk estimates. (Pfeiffer RM, Mbulaiteye S, Engels E. A model to estimate risk of infection with human herpesvirus 8 associated with transfusion from cross-sectional data. *Biometrics* 2004;60:249-56)

Loss of Antigenicity in Tissue Microarrays

The recent development of the tissue microarray (TMA) technique allows for standardized, rapid, and cost-effective immunohistochemical characterization of many cases of breast cancer and can be used to identify subtypes with distinct etiology. To evaluate whether staining intensity declines in whole sections prepared from conventional paraffin blocks with storage time (resulting in false-negative results), a single TMA block from 125 invasive breast carcinomas was analyzed. Estrogen receptor (ER)-alpha, progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression in sections cut and stored for six months at room temperature were compared with sections cut from the same TMA block and stained on the same day. Percentage of positive cases for stored versus fresh sections was similar for ER (59 percent) but significantly higher in fresh sections for PR (56 versus 64 percent, $p = 0.01$) and HER2 (46 percent versus 64 percent, $p < 0.001$). Among cases positive in both stored and fresh sections, the median percentage of immunoreactive cells was significantly reduced and the staining intensity was consistently lower in stored compared with fresh sections. Loss of immunoreactivity is an important problem in TMAs of breast cancer. (Fergenbaum JH, Garcia-Closas M, Hewitt SM, Lissowska J, Sakoda LC, Sherman ME. Loss of antigenicity in stored sections of breast cancer tissue microarrays. *Cancer Epidemiol Biomarkers Prev* 2004;13:667-72)

OBESITY

Obesity Appears to Increase Cancer Risk Among Black and White Men

Obesity has been linked to excess risk for many cancers, but the evidence remains tenuous for some types and few studies have included nonwhite subjects. The risk for all major cancer sites and subsites was examined among a cohort of male U.S. veterans (3,668,486 whites; 832,214 blacks) hospitalized with a diagnosis of obesity. Among white veterans, risk was significantly elevated for several cancers, including cancers of the lower esophagus, gastric cardia, small intestine, colon, rectum, gallbladder and ampulla of vater, male breast, prostate, bladder, thyroid, and connective tissue, and for malignant melanoma, multiple myeloma, chronic lymphocytic leukemia (CLL), and acute myeloid leukemia (AML). Excess risks initially observed for cancers of the liver and pancreas persisted among men without a history of diabetes or alcoholism. Among black veterans, risks were significantly elevated for cancers of the colon, extrahepatic bile ducts, prostate, and thyroid, and for malignant melanoma, multiple myeloma, CLL, and AML. **(Samanic C, Gridley G, Chow WH, Lubin J, Hoover RN, Fraumeni JF Jr. Obesity and cancer risk among white and black United States veterans. *Cancer Causes Control* 2004;15:35-43)**

OVARIAN CANCER

Survival Among Women with Borderline Ovarian Tumors

Serous and mucinous ovarian tumors of low malignant potential (LMP-S and LMP-M, respectively) are noninvasive tumors that portend excellent survival when confined to the ovary. Survival rates for women with borderline ovarian tumors and with ovarian cancer were compared. Relative survival rates at 10 years were 97 percent for LMP-S tumors, 30 percent for serous carcinoma (CA-S), 94 percent for LMP-M tumors, and 65 percent for mucinous carcinoma (CA-M). The survival rate at 10 years for women with distant-stage LMP-S tumors was 90 percent compared with 96 percent for women with well-differentiated, localized CA-S. The survival rate for women with distant-stage LMP-M tumors at five years was 86 percent compared with 96 percent for women with well-differentiated, localized CA-M (Figure 2). Mucinous ovarian neoplasms were associated with an excess of second malignancies of the digestive tract, including esophagus, stomach, small and large intestine, rectum, pancreas, and biliary tract. Relative survival among women with distant-stage LMP tumors resembled the survival of women who had carcinoma exhibiting favorable prognostic features (localized stage). **(Sherman ME, Mink PJ, Curtis R, Cote TR, Brooks S, Hartge P, Devesa S. Survival among women with borderline ovarian tumors and ovarian carcinoma: A population-based analysis. *Cancer* 2004;100:1045-52)**

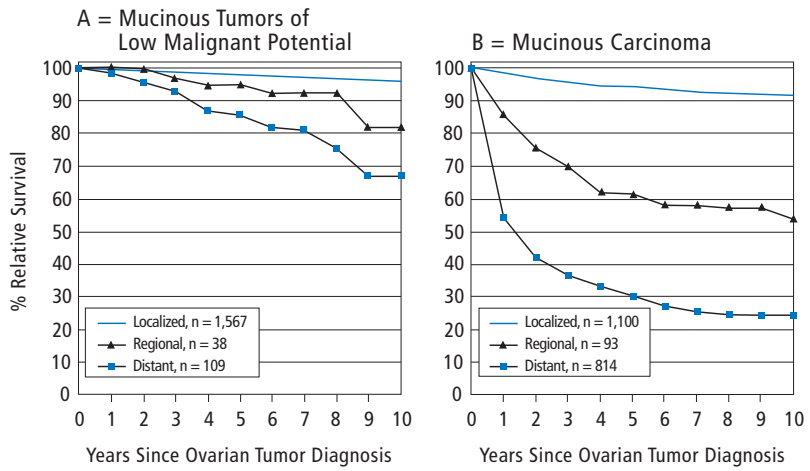


Figure 2: Cumulative relative survival for women with (A) mucinous tumors of low malignant potential (LMP-M) and (B) mucinous carcinoma (CA-M). Survival for women with either localized LMP-M or CA-M was greater than 90 percent. Women who had regional-stage or distant-stage LMP-M fared worse compared with women who had localized CA-M.

Ovarian Cancer Risk After Use of Ovulation-Stimulating Drugs

A retrospective cohort study of 12,193 eligible study subjects (median age 30 years), who were evaluated for infertility during the period of 1965 to 1988 at five clinical sites, identified 45 subsequent ovarian cancers. The infertility patients had a significantly elevated ovarian cancer risk compared with the general population (standardized incidence ratio = 1.98; CI = 1.4–2.6). When patient characteristics were taken into account and risks assessed in the infertile women, the rate ratios (RR) associated with ever use were 0.82 (CI = 0.4–1.5) for clomiphene and 1.09 (CI = 0.4–2.8) for gonadotropins. There were higher but nonsignificant risks with follow-up time. Although drug effects did not vary by causes of infertility, a slightly higher risk was associated with clomiphene use among women who remained nulligravid, based on six exposed patients (RR = 1.75; CI = 0.5–5.7). These results do not confirm the strong link reported in some studies between ovulation-stimulating drugs and ovarian cancer. Slight but nonsignificant elevations in risk associated with drug use among certain subgroups of users, however, support the need for continued monitoring of long-term risks. **(Brinton LA, Lamb EJ, Moghissi KS, Scoccia B, Althuis MD, Mabie JE, Westhoff CL. Ovarian cancer risk after the use of ovulation-stimulating drugs. *Obstet Gynecol* 2004;103:1194-1203)**

PANCREATIC CANCER

Cigars and Smokeless Tobacco and Risk of Pancreatic Cancer

A population-based case-control study was conducted among 154 subjects with newly diagnosed carcinoma of the exocrine pancreas and 844 population controls. Increased risks for pancreatic cancer were observed among those who smoked at least one cigar/week for 6 months or more (OR = 1.7; CI = 0.9–3.3), among those who smoked more than one cigar/day (OR = 1.8; CI = 0.8–4.2), and among those who smoked cigars for more than 20 years (OR = 1.9; CI = 0.9–3.9). In addition, subjects who regularly used smokeless tobacco had a 40 percent increased risk of pancreatic cancer (CI = 0.5–3.6) compared with nonusers of tobacco. Risk was increased among subjects who used more than 2.5 oz of smokeless tobacco/week (OR = 3.5; CI = 1.1–11), and long-term use of smokeless tobacco (i.e., > 20 years) was associated with a nonsignificant increased risk (OR = 1.5; CI = 0.6–4.0). In contrast, pipe smokers experienced no excess risk. These results suggest that heavy use of smokeless tobacco and, to a lesser extent, cigar smoking may increase the risk of pancreatic cancer among nonsmokers of cigarettes. **(Alguacil J, Silverman DT. Smokeless and other noncigarette tobacco use and pancreatic cancer: A case-control study based on direct interviews. *Cancer Epidemiol Biomarkers Prev* 2004;13:55-8)**

Nitrates in Drinking Water and Pancreatic Cancer

N-nitroso compounds, which are known animal carcinogens, are formed endogenously from intake of nitrate and nitrite. A population-based study of 189 pancreatic cancer cases and 1,244 controls in Iowa was conducted to determine whether increased consumption of nitrate and nitrite from drinking water and dietary sources was associated with risk. No association was observed between pancreatic cancer risk and increasing quartiles of nitrate in community water supplies. Increasing intake of dietary nitrite from animal sources, however, was associated with significantly elevated risks among men (highest quartile OR = 2.3, CI = 1.1–5.1) and women (OR = 3.2, CI = 1.6–6.4). In contrast, dietary nitrate intake showed no positive association with risk among men or women. Thus, long-term exposure to drinking-water nitrate at levels below the maximum contaminant level of nitrate nitrogen (10 mg/liter) is not associated with pancreatic cancer, but the consumption of dietary nitrite from animal products may increase risk. **(Coss A, Cantor KP, Reif JS, Lynch CF, Ward MH. Pancreatic cancer and drinking water and dietary sources of nitrate and nitrite. *Am J Epidemiol* 2004;159:693-701)**

PEDIATRIC CANCER

Childhood Tumor Risk after Maternal Ovulation-Stimulating Drugs

To assess childhood cancer risk among children conceived following the use of ovulation-stimulating drugs, a study was conducted among 30,364 Danish women evaluated for infertility beginning in the early 1960's. A total of 51 cancers were identified among the study children (standardized incidence ratio [SIR] = 1.14; CI = 0.8–1.5). There was no increased risk of childhood tumor observed with the use of any fertility drug (rate ratio [RR] = 0.82; CI = 0.4–1.6) or specifically with clomiphene citrate (RR = 0.77; CI = 0.4–1.6). Tumors occurring early in life and non-hematopoietic malignancies (including neuroblastomas) were not associated with drug use. Nonsignificant elevations in the risk of cancers occurring later in life, especially childhood hematopoietic malignancies (RR for use of any ovulation-stimulating drugs = 2.30, CI = 0.8–6.6), may have been related to the underlying reasons for medication use. The findings of this study suggest no association between maternal use of ovulation drugs and childhood cancer, but additional adequately powered studies are needed. **(Brinton LA, Kruger Kjaer S, Thomsen BL, Sharif HF, Graubard BI, Olsen JH, Bock JE. Childhood tumor risk after treatment with ovulation-stimulating drugs. *Fertil Steril* 2004;81:1083-91)**

RADIATION

Thyroid Cancer Among Children Exposed to I-131 after the Chornobyl Accident

In children, the thyroid gland is one of the organs most sensitive to external exposure to x- and gamma rays. Data on the risk of thyroid cancer in children after exposure to radioactive iodines are sparse, however. The Chornobyl accident in Ukraine in 1986 led to the exposure of large populations to radioactive iodines, particularly I-131. A trinational collaborative cohort study being conducted in Belarus and Ukraine includes 25,161 subjects younger than age 18 in 1986. Study subjects are screened for thyroid diseases every two years and individual thyroid doses are estimated based on 1986 measurements of thyroid gland radioactivity, along with a radioecological model and interview data. Approximately 100 histologically confirmed thyroid cancers were detected in the first round of screening. These data will enable fitting appropriate dose-response models, which are important in radiation epidemiology and public health for predicting risks from exposure to radioactive iodines from medical sources and possible future nuclear accidents. The cohort will be followed for at least three screening cycles, which will lead to more precise risk estimates. **(Chornobyl Thyroid Diseases Study Groups of Belarus, Ukraine, and the United States. A cohort study of thyroid cancer and other thyroid diseases after the Chornobyl accident: Objectives, design and methods. *Radiat Res* 2004;161:481-92)**

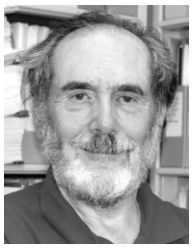
DCEG PEOPLE IN THE NEWS

Dalsu Baris, M.D., Ph.D., of the Occupational and Environmental Epidemiology Branch (OEEB), was invited to serve on the Scientific Board of Advisors to the International Myeloma Foundation (IMF) for the Bank on a Cure Project. IMF is a nonprofit organization dedicated to improving the lives of multiple myeloma patients. The Bank on a Cure Project will establish a comprehensive DNA repository from myeloma patients for epidemiologic and clinical research *(http://myeloma.org/myeloma/home.jsp)*. Dr. Baris made a presentation on molecular epidemiology and multiple myeloma at the board's recent meeting in Bermuda.

Sonja Berndt, Pharm.D., a predoctoral fellow in OEEB, received the Louis I. and Thomas D. Dublin Award in Epidemiology and Biostatistics from Johns Hopkins University for her proposal, "A comparison of approaches for estimating haplotype-disease associations."

Louise Brinton, Ph.D., Hormonal and Reproductive Epidemiology Branch (HREB), spoke on "Interpreting epidemiologic findings: Hormones and cancer risk," at the 5th International Symposium on Women's Health and Menopause, held in Florence, Italy, in April, and on "Cancer risk associated with causes of and treatments for infertility" at the Danish Cancer Registry in Copenhagen, also in April.

Melinda Butsch Kovacic, Ph.D. (HREB), has been selected as the editor for POSTDOCket, the quarterly newsletter for the National Postdoctoral Association *(http://www.nationalpostdoc.org)*.

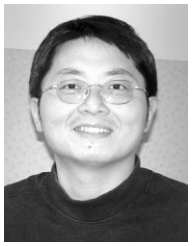

Kenneth Cantor

Kenneth Cantor, Ph.D. (OEEB), gave an invited talk on "Ingested arsenic and cancer epidemiology" at the American Association for the Advancement of Science meeting in Seattle in February.


Jim Vaught receives 2004 Distinguished Alumnus Award from Elizabeth Leibach, President of the Medical College of Georgia School of Graduate Studies Alumni Association

Jim Vaught, Ph.D. (Office of the Director), gave the keynote address at the U.S. meeting of the International Society for Biological and Environmental Repositories in New York City in May. He spoke on "Large biorepositories: Are there smarter ways to collect and store specimens?" Dr. Vaught also was selected to receive the 2004 Distinguished Alumnus Award from the School of Graduate Studies at the Medical College of Georgia, where he completed a Ph.D. in biochemistry in 1976.

Philip Castle, Ph.D. (HREB), spoke on "Human papillomavirus (HPV) and cervical cancer" at the University of Hawaii School of Medicine, and on "Practical applications concerning HPV carcinogenesis in screening and development: Vaccine development" at the International Association of Dental Research meeting in Honolulu in March.


Shih-Chen Chang

Shih-Chen Chang, Ph.D., Nutritional Epidemiology Branch (NEB), received an American Society of Preventive Oncology (ASPO) new investigator award for his abstract on "Association of dietary fat and colorectal adenoma." Dr. Chang presented this research and "Interrelation of energy intake, body size, and physical activity with postmenopausal breast cancer in the PLCO Screening Trial" at the ASPO meeting in Bethesda in March.

Eric Engels, M.D., Viral Epidemiology Branch (VEB), spoke on "Polyomavirus and childhood cancer" at the Children's Oncology Group meeting in Washington, DC, in April.

Mary Fraser, R.N., M.A., Genetic Epidemiology Branch (GEB), gave an invited presentation on "Education through publication" at the Dermatology Nurses' Association 2004 Skin Cancer Workshop in Orlando in March. Ms. Fraser also was appointed to the *Dermatology Nursing* editorial board.

Mitchell Gail, M.D., Ph.D., Biostatistics Branch (BB), spoke on "Preparing statisticians for research at the National Institutes of Health" at the Eastern North American Regional meeting of the American Statistical Society in Pittsburgh in March.

Michael Hauptmann, Ph.D. (BB), gave talks on cancer and formaldehyde at the Toxicology Forum Winter Meeting in Washington, DC, in February, and at the Department of Environmental and Occupational Health Sciences, University of Washington, in Seattle in April. Dr. Hauptmann also spoke on "Gene-environment interactions in case-control designs," at the Department of Epidemiology and Preventive Medicine at the University of Maryland in Baltimore in February.

Sadie Hutson, Ph.D., C.R.N.P., Clinical Genetics Branch (CGB), was selected to receive the Virginia Henderson Clinical Research Grant from Sigma Theta Tau International (the Honor Society of Nursing). The award is given to one recipient each year and helps fund study-related expenses.


Ruth Kleinerman

Ruth A. Kleinerman, M.P.H. (REB), gave an invited lecture on "Second cancer risk following radiotherapy" at the Radiation Research Society meeting in St. Louis, MO, in April.


Qing Lan

Qing Lan, M.D., Ph.D. (OEEB), and **Neil Caporaso, M.D.** (GEB), participated in the first meeting to form an international lung cancer consortium, which took place at the American Association for Cancer Research (AACR) meeting in Orlando in March. Dr. Lan presented a history of DCEG studies in Xuan Wei, China, that identified the study of the molecular epidemiology of lung cancer in nonsmoking women as one of the highest-priority research areas.

Michael Leitzmann, M.D., Dr. P.H. (NEB), gave invited presentations in January on "Diet and lifestyle factors in relation to prostate cancer risk" at the International Agency for Research on Cancer in Lyon, France, and at the German National Cancer Institute in Heidelberg.

Unhee Lim, Ph.D. (NEB), was invited to speak at the ASPO New Investigators workshop in Bethesda in March. Dr. Lim talked on "A biomarker study of one-carbon metabolism and colorectal adenoma in the CONCeRN (Colorectal Neoplasia Screening with Colonoscopy in Asymptomatic Women at Regional Navy/Army Medical Centers) Study." She gave a second oral presentation at ASPO on "Dietary B vitamins and the risk of lymphoid cancers in male smokers."

Roxana Moslehi, Ph.D. (BB), gave an invited presentation on cancer and developmental issues in the xeroderma pigmentosum heterozygote study at the American Academy of Dermatology meeting in Washington, DC, in February. Dr. Moslehi also spoke on "Cancer risks associated with DNA repair genes" at the Johns Hopkins Bloomberg School of Public Health, also in February.

Thomas O'Brien, M.D. (HREB), gave a lecture on "Genomics and proteomics: Promises and pitfalls" at the 35th Anniversary Meeting of the Southeastern Organ Procurement Foundation in Richmond in March. Dr. O'Brien moderated the session on "Pathogenesis" at a meeting on hepatocellular carcinoma at NIH in April.


June Peters

June Peters, M.S., C.G.C. (CGB), coauthored "Genetic cancer risk assessment and counseling: Recommendations of the National Society of Genetic Counselors (NSGC)," which appeared in the April 2004 issue of *Journal of Genetic Counseling*. This is the first set of guidelines on cancer risk produced by the NSGC *(http://www.nsgc.org/)*.

Margaret Tucker, M.D. (GEB), gave an "Overview of genetic epidemiology" at the first NCI–King Hussein Cancer Center Conference and the 4th Jordan Oncology Society Conference, which were held in Amman, Jordan, in April. She also gave two talks at St. James Hospital in Dublin, Ireland, in March on "Challenges and opportunities in genetic epidemiology" and "Genetic epidemiology of melanoma." In addition, Dr. Tucker was inducted into the American Epidemiological Society in March.


Margaret Tucker (center) at the NCI-King Hussein Cancer Center Conference in Amman, Jordan, along with Otis Brawley (left) from Emory University School of Medicine, and Michael Friedman (right) from City of Hope National Medical Center

Charles Rabkin, M.D. (VEB), gave an invited talk on "The molecular epidemiology of Kaposi's sarcoma and other AIDS-related malignancies" to the Uganda Society of Health Scientists in March. Dr. Rabkin and **Sam Mbulaiteye, M.D.** (VEB), also participated in the Annual Conference of Physicians of Uganda.

Preetha Rajaraman, Ph.D. (REB), was inducted into Delta Omega, a national honorary society for graduate students in public health, in May.


Tanuja Rastogi

Tanuja Rastogi, Sc.D.(NEB), gave an oral presentation on "Diet and risk of biliary tract cancers: A population-based study in Shanghai, China," at the ASPO meeting held in Bethesda in March. This paper was selected as one of the top meeting abstracts.

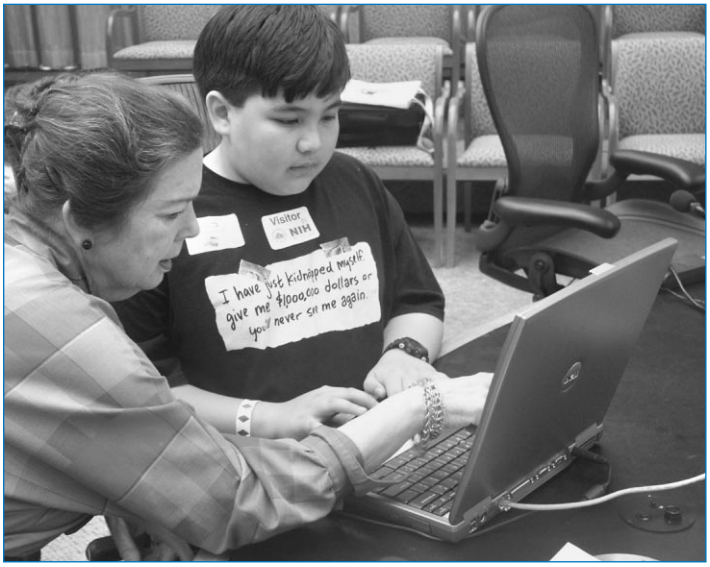

Cecile Ronckers

Cecile Ronckers, Ph.D. (REB), received the Brigid G. Leventhal Scholar Award in Cancer Research from the AACR Women in Cancer Research group in Orlando in April for her work on "Second primary thyroid cancer after a first childhood malignancy." Dr. Ronckers also delivered a lecture on "Radiation and cancer" at the University of Maryland in April.

Nathaniel Rothman, M.D. (OEEB), chaired a meeting of the Genetic Polymorphism Working Group of InterLymph, an international consortium of non-Hodgkin's lymphoma (NHL) studies, held at the AACR meeting in Orlando in March. At the meeting, **Sophia Wang, Ph.D.** (HREB), and Qing Lan, presented preliminary results from a meta-analysis of single nucleotide polymorphisms from eight NHL case-control studies. This represents one of the first consortia efforts to study common genetic variants and cancer risk.

Arthur Schatzkin, M.D., Dr.P.H. (NEB), spoke on "Problems with using biomarkers as surrogate end points for cancer" at the Controversies in Tumor Prevention and Genetics conference in St. Gallen, Switzerland, in February. Dr. Schatzkin also gave presentations on nutrition and cancer at the American Epidemiological Society meeting in Seattle in March, and at the Albert Einstein College of Medicine, New York, in April.

Lois Travis, M.D., Sc.D. (REB), served on the faculty for an American Society of Clinical Oncology's educational symposium called "The Price of Success: Long-term Complications of Treatment," during the annual meeting in New Orleans in June. Dr. Travis also gave an invited talk on "Second cancers: An overview" for Grand Rounds at the Memorial Sloan-Kettering Cancer Center in New York in April.



B.J. Stone teaches at NIH Take Our Sons and Daughters to Work Day


Gloria Gridley teaches at NIH Take Our Sons and Daughters to Work Day

Gloria Gridley, M.S., and **B.J. Stone, Ph.D.** (BB), led a session at the NIH Take Our Sons and Daughters to Work Day in April. Under their guidance, students surfed the NCI Cancer Atlas web site and viewed U.S. cancer mortality maps. Students were taught how epidemiologists use these maps to search for clues to cancer etiology.

Roel Vermeulen, Ph.D. (OEEB), gave a talk on "Exposure assessment: Dealing with variability" at the University at Albany School of Public Health, Department of Epidemiology, in April.


Mary Ward

Mary Ward, Ph.D. (OEEB), addressed the Texas School of Rural Public Health in Bryan, TX, on "Using GIS for exposure assessment of pesticides in drinking water" in April.


Robin Wilson

Robin Wilson, Ph.D. (OEEB), spoke on "The role of primary care patterns in stage at diagnosis outcomes among American Indian cancer patients" at the Pennsylvania State College of Medicine in Hershey in March.


Margaret Wright

Margaret Wright, Ph.D. (NEB), received a New Investigators Award and gave a presentation on "Elucidating the biological effects of B-carotene supplementation on lung carcinogenesis in male smokers" at the ASPO meeting in Bethesda in March. Dr. Wright also presented on "Effect of estimated renal net acid excretion on bladder cancer risk" at the Experimental Biology Annual Meeting in Washington, DC, in April.

INNOVATIVE PROPOSALS WIN INTRAMURAL RESEARCH AWARD

DCEG funds several Intramural Research Awards (IRAs) each year that recognize small, innovative, and interdisciplinary research projects. This year's winners are **Eric Engels, M.D., M.P.H.**, of the Viral Epidemiology Branch; **Montserrat Garcia-Closas, M.D., Dr.P.H.**, of the Hormonal and Reproductive Epidemiology Branch; and **Rachel Stolzenberg-Solomon, Ph.D., M.P.H.**, of the Nutritional Epidemiology Branch. All are DCEG tenure-track investigators.


DCEG Intramural Research Award Recipients: Eric Engels, Montserrat Garcia-Closas, and Rachel Stolzenberg-Solomon

Dr. Engels won for his proposal to investigate BK virus (BKV) in neuroblastoma. Neuroblastoma is the most common malignancy in infants. The etiology is unknown, but a recent study suggested that early-life infection with the BK polyomavirus might be a factor. Dr. Engels and his collaborators will seek to determine whether BKV can be detected in neuroblastoma tissue and to identify whether *in utero* or early-life transmission occurs in children who subsequently develop these tumors.

Dr. Garcia-Closas was recognized for her proposal to validate the use of pooled DNA to identify associations between genetic polymorphisms and bladder cancer risk. Using pooled DNA samples from many individuals rather than individual samples to obtain estimates of allele frequencies (allelotyping) is a promising approach to efficiently screening large numbers of single nucleotide polymorphisms (SNPs) for their association with cancer risk. Using samples from a study of bladder cancer, Dr. Garcia-Closas will develop and validate 500 allelotyping assays at the NCI Core Genotyping Facility. This technology will then be applied to screen for potentially relevant SNPs in key pathways that may lead to bladder cancer.

Dr. Stolzenberg-Solomon won for her proposal to evaluate endogenous sex hormones in postmenopausal women during weight loss and weight loss maintenance. An estimated 25 percent of breast cancer cases may be attributable to obesity and sedentary lifestyle, putatively through mechanisms that alter endogenous hormones. This project will be ancillary to the extramural National Heart, Lung, and Blood Institute study, The Weight Loss Maintenance Trial.

In the IRA program, tenure-track investigators and fellows in the Division apply for funds (up to $75,000 per year, renewable for up to three years) for small projects that cross usual organizational boundaries. Each proposal is reviewed by a member of the NCI Board of Scientific Counselors or another scientist from outside NIH with appropriate expertise, plus senior DCEG scientists. The proposals are judged with respect to their 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 resources, and programmatic relevance to the Division. The award can be combined with funds from other sources to support a larger project.

COMINGS…GOINGS

Michelle Althuis, Ph.D., a postdoctoral fellow in the Hormonal and Reproductive Epidemiology Branch (HREB) since 2001, has accepted an Assistant Professor position at Georgetown University Lombardi Comprehensive Cancer Center. While in DCEG, she studied exogenous exposures and hormone-related cancer etiology. She also evaluated cancer risk following ovulation-stimulating drug use and breast cancer risk associated with oral contraceptives.


Gabriella Andreotti

Gabriella Andreotti, M.P.H., has joined HREB as a predoctoral fellow. Ms. Andreotti, a doctoral student at the George Washington University (GWU) School of Public Health, will conduct dissertation research on the role of genetic susceptibility in biliary tract cancer. Ms. Andreotti received an M.P.H. degree in epidemiology from GWU in 1998. Since then, she has carried out epidemiologic surveillance and research in the Army Medical Surveillance Program at the Walter Reed Army Medical Center.


Andrea Baccarelli

Andrea Baccarelli, M.D., Ph.D., Genetic Epidemiology Branch (GEB), left DCEG in May. Dr. Baccarelli returned to Italy to accept an appointment as Assistant Professor in the Department of Occupational and Environmental Health at the University of Milan. He will work in the Research Center on Occupational, Environmental and Clinical Epidemiology and will focus on molecular epidemiology.

Kaye Brock, Ph.D., a senior lecturer in the School of Behavioral and Community Health Sciences at the University of Sydney in Australia, is spending a five-month sabbatical in the Biostatistics Branch (BB).

Sylvia Cameraro, M.Sc., an industrial hygienist from the University Institute of Oncologia of the Principality of Asturias in Spain, is visiting the Occupational and Environmental Epidemiology Branch (OEEB) for three months. She will assess chemical exposures identified in the Spanish Bladder Cancer Study.


Sophie Fossa

Sophie Fossa, M.D., Ph.D., of the Norwegian Radium Hospital and the University of Oslo, is a Visiting Scientist in the Radiation Epidemiology Branch until August. As a clinical oncologist and radiotherapist, Dr. Fossa has a special interest in survivorship issues and is collaborating with Dr. Lois Travis and colleagues on international studies of second cancers and mortality among survivors of testicular cancer and Hodgkin's lymphoma.


Carsten Hirt

Carsten Hirt, M.D., has joined the Viral Epidemiology Branch as a visiting fellow. For his medical thesis, he conducted research on detecting minimal residual disease in low-grade non-Hodgkin's lymphoma (NHL) by real-time quantitative polymerase chain reaction. Before coming to NCI, he was a clinical fellow in the Department of Hematology and Oncology at the University of Greifswald in Germany. Dr. Hirt will work on determining correlates and predictors of peripheral blood mononuclear cells bearing NHL-associated translocations, and the relationship of these mutations to the risk of NHL among subjects with advanced HIV infection and in the general population.


Kimberly Kerstann

Kimberly Kerstann, Ph.D., has joined GEB as a postdoctoral fellow. Dr. Kerstann received a doctoral degree in genetics and molecular biology from Emory University in 2003. Before coming to DCEG, she was a postdoctoral fellow at the National Human Genome Research Institute, where she studied the variability of methylation patterns in the promoter region of cancer-associated genes. Dr. Kerstann will apply her experience in identifying susceptibility genes/risk factors in association studies to the field of cancer genetics. She is working on analyses of family history of cancer among relatives of glioma cases from the DCEG case-control study of brain tumors.


Larissa Korde

Larissa Korde, M.D., M.P.H., has joined the Epidemiology and Biostatistics Program as a Cancer Prevention fellow. Dr. Korde received a medical degree from New York Medical College and completed her internal medicine residency at Georgetown University. She is now finishing oncology subspecialty training at NCI and will work on analyses of soy intake during childhood, adolescence, and adult life. Dr. Korde is also working on clinical intervention trials to reduce breast cancer risk through physical activity at NCI's Center for Cancer Research.

Srmena Krstev, M.D., Ph.D., has returned to the Institute of Occupational and Radiological Health in Belgrade, Yugoslavia, after completing a sabbatical year in OEEB. While in DCEG, Dr. Krstev evaluated occupational exposures associated with nonmalignant respiratory disease in the Shanghai Women's Cohort. She also evaluated the mortality experience among a cohort of workers employed in the U.S. Coast Guard Shipyard in Baltimore.


Mark Purdue

Mark Purdue, Ph.D., has joined OEEB as a visiting fellow. Dr. Purdue recently completed a doctoral degree in epidemiology at the University of Toronto. His dissertation research examined risk factors for *p*53 protein abnormalities in malignant melanoma. During his fellowship, Dr. Purdue plans to study hormone replacement therapy and adenomatous polyps in the PLCO trial, and environmental tobacco smoke and colorectal cancer in the Shanghai Women's Cohort.

Isela Velazquez, M.D., completed an M.P.H. fellowship in the Clinical Genetics Branch and has accepted a position as an Associate Medical Director with AstraZeneca in Wilmington, DE. During her DCEG fellowship, Dr. Velazquez worked on a prospective analysis of the penetrance of *BRCA1* and *BRCA2* mutations in hereditary breast/ovarian cancer. She also worked on the role of androgens in liver tumors among individuals with and without Fanconi's anemia.


Ulrike Peters

Ulrike Peters, Ph.D., a postdoctoral fellow in the Nutritional Epidemiology Branch, left DCEG in May to take a faculty position at the Fred Hutchinson Cancer Research Center at the University of Washington in Seattle. During her fellowship, Dr. Peters worked on molecular epidemiology studies of nutritional exposures in relation to colorectal and prostate cancer risk. She was involved with the Navy Colorectal Adenoma Study, the Beltsville Feeding Study, and the Swedish In-Patient Registry, and played a pivotal role in managing the etiologic component of the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Trial.

BETH MALONEY JOINS CDC


Elizabeth Maloney joins CDC

Elizabeth (Beth) Maloney, Dr.P.H., who worked in the Viral Epidemiology Branch for 21 years, left DCEG in February to join the Centers for Disease Control and Prevention in Atlanta. Dr. Maloney started at NCI in 1983 as an epidemiology research assistant in what was then the Viral Epidemiology Section. With an undergraduate degree in psychology, she knew she wanted to pursue work in the public health field. That pursuit eventually led to an M.S. degree in biostatistics from Georgetown University and a doctoral degree in public health in 2001 from the Uniformed Services University of the Health Sciences.

"DCEG's support of my education and training made my many years at NCI an ever-changing experience by providing new opportunities for professional growth," said Dr. Maloney. "In particular, Dr. Bill Blattner took the first chance on me by bravely supporting my master's degree, and Dr. Angela Manns and Dr. Jim Goedert gave me the time to complete coursework for my doctoral training. I am grateful not only for their selfless choices but also for their belief in me."

Over the years, Dr. Maloney focused her research on the study of human T-cell lymphotrophic virus (HTLV). She was a lead investigator on the Jamaican Mother-Infant Cohort Study of HTLV-I and on the Study of HTLV-II in the Guaymi Amerindians of Panama. She and her Jamaican colleagues reported HTLV-I–associated conditions in children. Working with Dr. Ruthann Giusti and collaborators from Panama, she described sexual risk factors for HTLV-II infection in the Guaymi. Dr. Maloney also serves as an editorial reviewer for several journals, including the *International Journal of Epidemiology* and the *Journal of Infectious Diseases*.

Dr. Maloney now is an epidemiologist at the National Center for Infectious Diseases in the Division of Viral and Rickettsial Diseases. She works with Dr. William Reeves on studies of chronic fatigue syndrome and with Dr. Elizabeth Unger on studies of human papillomavirus and cervical cancer.

DIVISION ALUMNI GIVE CAREER SEMINAR

DCEG welcomed back four division alumni for a Careers in Epidemiology Seminar held April 15. Drs. Emily Harris, Elizabeth Harvey, Daniel Hoffman, and Sandra Melnick spoke of the application of epidemiology in their positions in managed health care, the pharmaceutical industry, academia, and the Federal government. **Shelia Zahm, Sc.D.**, Deputy Director of DCEG and organizer of the seminar, stressed the importance of helping direct DCEG fellows to numerous opportunities in the epidemiology field because more than 75 percent of Division fellows will leave NCI to pursue their careers.

Careers in Epidemiology: (front) Emily Harris, Shelia Zahm, Elizabeth Harvey; (back) Sandra Melnick and Daniel Hoffman

Dr. Harris, a DCEG staff fellow from 1984 to 1986, is an assistant program director at the Kaiser Permanente Center for Health Research in Portland, OR. "My experience at NCI introduced me not only to epidemiology but specifically to cancer epidemiology and genetics," noted Dr. Harris, whose research focuses on the role of genetics in a variety of diseases. She works on projects with diverse approaches, including clinical trials, effectiveness trials, observational epidemiology studies, health services delivery, and health economics.

Dr. Harvey spent 1980 to 1986 at DCEG as a predoctoral and postdoctoral fellow before moving to a career in the pharmaceutical industry. She is Director of the Oncology Business Unit at Sanofi-Synthelabo, Inc. In that position, she helped launch two new oncology drugs and played key roles in all stages of the drug development, clinical testing, and marketing process. Dr. Harvey reflected that she was led into an industry career by the silver-bullet concept of antibody drug development nearly 20 years ago. "The industry world is fast-paced and exciting but often [has] unforgiving deadlines," noted Dr. Harvey. She encouraged fellows to explore the many career opportunities in medical industry for epidemiologists.

Dr. Daniel Hoffman, Associate Dean of the George Washington University (GWU) School of Public Health and Health Policy and Professor of Epidemiology and Biostatistics, spoke about his experiences in academia. After spending six years conducting radiation epidemiology studies at DCEG, Dr. Hoffman joined the Centers for Disease Control and Prevention in 1986, and moved to GWU in 1994. As the M.P.H. Program Director, he has played a lead role in developing the new school of public health. He stressed the importance of teaching in academia and strongly encouraged fellows to gain teaching and mentoring experience and welcomed audience members to give guest lectures at GWU. Dr. Hoffman still collaborates with DCEG on the study of Russian workers in a nuclear facility.

Dr. Sandra Melnick spent several years in academia before coming to NIH in 1992, first as an epidemiologist with the National Institute of Allergy and Infectious Diseases and then in NCI's extramural research program in epidemiology and genetics, which was part of DCEG before its reorganization into the Division of Cancer Control and Population Sciences. In her position as Chief of the Analytic Epidemiology Research Branch, she oversees a branch portfolio with a budget of more than $180 million annually and more than 450 funded projects. Dr. Melnick said that she enjoys her job of being "a guide through the NIH black box for principal investigators." Rather than doing research, she takes great satisfaction in helping build the science careers of others and set future directions for the field. ■